Congress of the United States
Office of Technology Assessment

INFERTILITY: MEDICAL AND SOCIAL CHOICES

Contractor Documents

Volume IV: Social and Medical Concerns

February 1988

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J952-18

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THE PSYCHOLOGICAL ASPECTS OF BEING INFERTILE

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This work has been performed for and submitted to the Office of Technology Assessment.

ACKNOWLEDGMENTS

The author gratefully acknowledges the help of a number of individuals who contributed to the information contained in this document.

Elizabeth Ann Hales provided hours of time and expertise as she interviewed staff members at the invitro fertilization clinics and Veterans' Administration Hospitals listed in Appendix A. The Ferre Institute in Utica, N.Y. was most generous in providing access to data from over 300 infertile couples and in making publications on infertility available to the author. Conversations with Beverly Freeman and Diane Clapp at National RESOLVE were extremely helpful in adding depth and breadth to material contained in the document. Yvonne Sterling's computer assistance contributed substantially to the ease with which this document was prepared.

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INTRODUCTION

Infertility is the inability to conceive a pregnancy after a year or more of regular sexual relations without contraception or the incapacity to carry pregnancies to a live birth. More than ten million people, or about one in every six couples of childbearing age in the United States, are infertile. These couples, most of whom had presumed themselves to be fertile and many of whom had conscientiously practiced birth control until they were ready to begin their families, find that the diagnosis of infertility represents a severe jolt to their life hopes and dreams. For many of these couples, efforts at diagnosis will be time consuming and costly, adding to their already present emotional stress. Once a diagnosis is reached, the couple then faces decisions about their future that again place in doubt the ease with which they will be able to expand their family. Some couples have infertility conditions that will not respond to treatment, and for them the emotional task ahead involves mourning the loss of the birthchild that they never can have and then evaluating what future options are available to them. Other couples will be told that treatment is available for their infertility, although the outcome may be uncertain. These couples must weigh the costs and risks of medical intervention against their desire for a birthchild. Although 50 percent of couples who enter into a proper investigation of their infertility will respond to treatment and conceive, the treatment experience itself can consume years of a couple's life and thousands of dollars of hard-earned savings. And, although couples who are helped to conceive will say that no sacrifice could be too great for the baby they finally hold in their arms, most of them carry the emotional scars of their infertility experience for years to come. For the 50 percent of couples unable to conceive despite treatment, the emotional pain is devastating. Having invested an immense amount of psychological energy, physical stamina, and financial cost in the effort to conceive, these couples are emotionally drained as they reach the painful decision to terminate treatment and re-evaluate other means by which children can be a part of their lives. For 10 percent of infertile couples, no reason can be identified for their inability to have a child. These couples are in a particularly vulnerable position, because neither they nor their physicians can identify factors that could increase their chances of conceiving a baby. Couples with unexplained (idiopathic) infertility are in a situation of emotional limbo - often wanting to try just "one more" treatment or wait just "one more" month, as they cling to the slender thread of hope that they can have a birthchild.

The emotional experience of infertility differs for each individual. Many clinicians perceive infertility as a life crisis that poses threats to self esteem, sexual identity, marital stability and life goals. Whereas literally hundreds of infertility clinics are offering medical services to couples, there is considerably less available in the way of emotional supports and resources for infertile people. Given the unique psychological issues and the tremendous emotional stress that most individuals experience in the course of grappling with their infertility, it is crucial to view infertility as a condition that requires both a medical and a psychological response.

THE PSYCHOLOGICAL ASPECTS OF BEING INFERTILE

PSYCHOLOGICAL PROFILE OF INFERTILE COUPLES

The Psychological Profile of an Infertile Male

Infertility in the male evokes a wide range of emotional reactions, depending upon the finality of the diagnosis, the investment of the male in becoming a birth parent, the cause of his infertility, his partner's response, and his readiness to confront the emotions that are evoked by the diagnosis of infertility.

If the male is strongly invested in becoming a birth parent, his response to learning of his infertility will be that of having sustained a tremendous loss. Any psychological attachment to the dreamchild he hoped to conceive with his partner will be dramatically altered, with the accompanying feelings of emptiness and sadness. For males who have been socialized not to express emotions associated with grief, there is likely to be more comfort in expressing the anger felt at being deprived of the role of being a birth parent. Such anger may be directed toward the self, which may result in depression, or it may be directed toward others: medical professionals, the fertile world, and even one's partner. It is not unusual for an infertile partner to fear actual or emotional abandonment by the fertile partner; some will continually test and provoke the partner with comments like "If you had married someone else, you would have a family by now" (Mazor, 1984). Although some authors report an increased incidence of extramarital affairs (Walker, 1978), others cite the more frequent loss of libido and depression (Mazor, 1984; Menning, 1977). Infertile males may lose interest in sex for awhile or have a temporary bout of impotence;

several authors have described temporary impotence as a problem in half of the infertile males in their studies (Mazor, 1980; Debrovner and Shubin-Stein, 1976; Walker, 1978). It is common for males to refer to their role in intercourse as "shooting blanks" (Mazor, 1984), which is a reflection of the low self esteem they feel as they associate virility with self worth.

For males who are less strongly invested in being birth parents, adoption or artificial insemination of their partner may be plausible options. For these males, the feelings of diminished self esteem may be channeled into efforts to excel in other areas: career, social relations, or volunteer activities. Leitko and Greil report that men seem to be less concerned with their inability to become parents than with their inability to make their wives happy or with their inability to maintain "normalcy" within their homes and their marital relationships. Although males may experience feelings of disappointment at being denied the opportunity to become a birth parent, in many cases their investment in this role is sufficiently flexible that they can move into exploring other ways of building a family, or filling the void of a childfree relationship, without actively grieving.

For some males, the cause of their infertility will play a function in their response. If the infertility is related to an infection contracted from sexual contact, there may be feelings of guilt about past behavior and anger that the result of carefree sexual contact is such a permanent setback to life hopes. Males who have undergone a vasectomy are likely to experience anger at themselves for not having been farsighted enough to anticipate that life plans and goals might change. If the male has fathered a child in a previous relationship, there may be an increased value placed on that child, at the very time that his female partner is hoping to consolidate their relationship through having a baby of their own. For males who have chosen to delay childbearing, there may be feelings of frustration that if and when a child is born the prospective father may not have as much energy to give to the demands of childrearing. On the other hand, males who have a condition over which they could have exerted no control are likely to be plagued with feelings of helplessness, but they are less likely to resort to self blame as a response to their infertility.

Males who are undergoing treatment for their infertility are likely to be engaging in some anticipatory mourning, as many male fertility problems are not as amenable to medical intervention as are problems in the female. If the treatment goes on for many months and even years, the male is likely to experience the process of chronic mourning in which he is unable to draw closure on his hopes for a birthchild, always hoping that the next treatment may be successful. On the other hand, the treatment of artificial insemination by donor, which holds promise if the infertile male is known to have a fertile partner, can cause a number of psychological issues to surface, particularly the awareness that his partner may become pregnant from another man's sperm. Males may wonder whether they are capable of the same feelings of love that they would have felt if their partner had given birth to a baby conceived from their sperm. It is not unusual to be preoccupied with questions about the donor and his characteristics.

The Psychological Profile of an Infertile Female

When the female is the partner with the infertility problem, there also occurs a range of psychological responses. Leitko and Greil report case-study and clinical evidence that shows infertile women to experience abnormally high levels of anxiety (Bell, 1981; Berk and Shapiro, 1984). Similar clinical reports depict infertility as a significant life crisis for women characterized by depression (Berk and Shapiro, 1984; Bresnick, 1981; Menning, 1982), impaired body image, narcissistic concentration on treatment, social and emotional withdrawal (Kraft, et al. 1980; Mazor, 1984) and greater guilt and more restrictive attitudes about sex (Slade, 1981). In a study of two hundred infertile couples, half the women and 15 percent of the men reported that infertility is the most upsetting experience of their lives (Freeman, Boxer, and Rickels et al., 1985). In addition to the responses detailed above for the infertile male, the female has some unique issues with which she must grapple. Since it is her body that would have nurtured a pregnancy, there is likely to be a strong sense of body betrayal. Women in today's society usually are well socialized about their reproductive health. From annual pelvic exams to monthly breastchecks to informed choices of birth control, the woman's concern about her reproductive health makes visits to a gynecologist an often-routine aspect of her general health care. Thus, when anxiety about her inability to conceive becomes more than just a topic of speculation between partners, it is usually the woman who initiates the request for medical help, and frequently it is she who undergoes many of the initial diagnostic procedures.

Wanting to trust one's body and yet feeling betrayed by it is a frequent complaint of infertile women who are still hoping to conceive. The woman experiences the anguish of not being able to distinguish premenstrual symptoms from symptoms of early pregnancy. Tender breasts, queasiness, and some abdominal discomfort can raise a woman's hopes and then plunge them precipitously. This monthly emotional rollercoaster takes a tremendous toll on both partners.

Another dimension of emotional stress a woman may experience has to do with side effects from drugs that are prescribed to increase her chances of conceiving. Weight gain, depression, hot flashes and acne are all concomitants of various medications and, at a time when many women are feeling at an emotional low ebb, medically induced discomforts only add to feelings of helplessness.

The emotional issue of guilt is unique for women. Since females experience their peak period of fertility in their twenties, a woman who begins trying to conceive when she is in her thirties or forties may blame herself for waiting "too long." Especially if the reason for the delay has been something the woman may later see as inconsequential (career, education, financial security, a house), the guilt at having let her peak fertile years slip by forever is a punitive emotional experience.

Other women look for, and often find, a variety of potential sources of self blame: an unwanted earlier pregnancy that was terminated, use of the intrauterine device and resultant pelvic inflammatory disease, a bout with one of the sexually transmitted diseases that impairs fertility, experimental drug use or substance abuse. Finding a plausible source of blame can cause the woman to punish herself emotionally, rather than to relegate the cause to past history and to focus on constructive steps that she and her partner can take in the present.

Ultimately, as both partners come to terms with their infertility, the issues of grief are unique ones for the woman. Although her male partner may grieve for his inability to pass on his genes to his offspring, the woman's grief tends to be more visceral as she mourns for the fetus she will never nourish during the nine months of pregnancy, as she feels left out while pregnant friends discuss their plans for labor and delivery, as she sees a nursing mother and quickly turns away. The physical emptiness is more intense for some women than for others, but it is clearly an emotional hurdle to surmount on the way to resolving the emotional upheaval caused by infertility.

Given the unique emotional needs that women experience, it is also relevant to examine the coping mechanisms that women develop to deal with this unanticipated life crisis. The preponderance of women who seek counseling for issues related to their infertility, the predominantly female attendance at RESOLVE meetings around the nation, and the experience of RESOLVE telephone counselors who report that an overwhelming percentage of their telephone calls is from females, reflect the greater willingness of women over their male partners to reach out for help during a time of emotional stress. This ability to initiate contact in an effort to ease the emotional burden of infertility speaks poignantly to the need women feel to validate their emotions by exploring them with someone who can offer support during a time that is stressful for males and females alike.

The Psychological Profile of the Fertile Partner in an Infertile Couple

Fertile partners offer a range of reactions to their mates' infertility. The response of the fertile partner will greatly influence the couple's capacity to acknowledge their sadness, to make decisions and to explore future life plans.

If the fertile partner is supportive and regards the mate's infertility as an unfortunate occurrence that disrupts their mutual life dreams, there is usually the opportunity for both of them to work together to resolve their emotions and to move ahead in the decision-making process. Some fertile partners, although accepting of their mates' infertility, are reluctant to discuss their own feelings of sadness for fear that they may make that mate feel guilty or somehow responsible. Mazor (1984) reports that the fertile partner may feel an obligation to maintain a front of unswerving loyalty and to disavow any disappointment or anger. This has the effect of cutting the couple off from open and honest communication and may cause the infertile partner to feel even more anxious. The couple's inability to communicate about their infertility can cause intense feelings of emotional isolation that may extend to relationships with significant others. It is fairly common for fertile and infertile females to isolate themselves from their male partners in an effort to disguise the extent of emotional pain they are feeling. Particularly in relationships where males have demonstrated a discomfort with tears and emotional outbursts, the woman may feel that she dare not risk sharing her most private emotions only to have her partner turn away.

In some couples the infertile partner will be verbally or behaviorally provocative in conveying the message that the fertile partner could have a baby in a different relationship, thereby calling into question the depth of the relationship and the investment in having a baby versus continuing the relationship. The fertile partner may respond to this testing behavior or may weather the emotional storm. In some cases the efforts of the fertile partner to reassure the infertile partner may prevent the fertile partner from acknowledging the actual emotions of being trapped, feeling angry, or even feeling immense sadness at their predicament.

If an individual is infertile because of an earlier sterilization, it is likely that the fertile partner was aware of this situation prior to their decision to have children. As a result, the infertility is not so much unanticipated as it is unwanted. The option of artificial insemination or invitro fertilization exists for some couples, if they feel strongly about having a birth child. Otherwise, adoption is another option that the couple may decide to pursue. If one partner had birthchildren in a previous relationship, it is possible that they are involved in the life of their parent and his/her new mate, and this may either prove a sense of pleasure or frustration for the childless partner. If the reason for the infertility is identified as related to a sexually transmitted disease, the fertile partner will probably feel anger at some level that the mate's lack of attention to sexual health results in their inability to bear a child. In other cases of infertility, the cause is unlikely to be one over which the individual could have had any control, making it harder for the fertile partner to identify the mate as responsible, although undoubtedly both will have the normal feelings of anger and sadness associated with not being able to pursue life dreams as easily as both of them had hoped.

In many circumstances there is disagreement between two partners regarding the medical efforts they are willing to pursue in order to conceive a child. If the fertile partner feels the infertile mate is resisting available treatment options, this impasse will create considerable stress in their relationship. It is not uncommon for the fertile partner's response to change over time, as the narcissistic blow of the couple's infertility is felt full force, and as coping mechanisms develop in response to what many couples perceive as a life crisis.

The Impact of Diagnosis on the Infertile Couple

In couples with infertility, women have the problem in 40 percent of the cases, men have the problem in 40 percent of the cases, and both partners share the problem in the remaining 20 percent of the cases (Menning, 1977). Regardless of which partner is responsible physiologically for the diagnosis of infertility, both partners must grapple with the psychological impact of their inability to conceive a baby or carry a pregnancy successfully to term. This is a devastating blow to couples who had looked forward to beginning a family and who subsequently feel as though their dreams have been shattered. Their ability to come to terms with the crisis of infertility will greatly influence their relationship as a couple, their social interactions with friends, co-workers and extended family members, as well as their capacity to look ahead to life options that may or may not include enlarging their family.

Untreatable Infertility

If the couple is told that their infertility is caused by a problem for which there is no medical cure, their psychological response is almost universally going to resemble that of mourning a death (Menning, 1977; Shapiro, 1982). The very fact that they have invested in an infertility workup indicates the importance their fertility holds for them. To learn that they are infertile and that they will never have a birthchild catapults them into a mourning process for the several losses they have sustained: first and foremost is the loss of their dreamchild, around whom they may already have begun to build fantasies and form an elusive attachment; second is the loss of reproductive health which, for some, translates into a feeling of body betrayal; third is the loss associated with the hopes of experiencing pregnancy, childbirth, and perhaps breastfeeding a baby; and last is the loss of becoming parents as easily as the couple had assumed would occur for them. Some of these losses will be more compelling for one partner than for the other; the pace of the mourning process also is likely to differ for each partner.

Treatable Infertility

When a couple receives the information that there is treatment available for their infertility, it is quite likely that they will have an ambivalent response. On one level there is both relief and hope that they have a problem that may be amenable to treatment and that allows them still to hold out the hope of one day delivering a healthy baby. On another level they feel apprehensive as they anticipate potentially difficult decisions if they have limited financial resources or must travel a long distance to receive treatment or must weigh the risks associated with various medical interventions. Finally, there is likely to be a residue of fear and apprehension as the couple realizes that the treatment may not be successful, and that their dreams of having a birthchild will never be realized. The task of the couple at the time that treatment is offered is to decide whether or not to embark on what may be a costly, disruptive, and psychologically stressful undertaking.

Shared Infertility

For 20 percent of infertile couples, the diagnostic workup reveals that both partners contribute to the infertility problem of the couple. For such couples, infertility indeed represents a challenge, both medically and emotionally. The response by physicians will have considerable impact on the emotional well-being of the couple. It is crucial that physicians be in close communication, with a team approach if possible. It is also important to communicate diagnostic impressions and treatment outcomes to both partners whenever possible, so that the couple with shared infertility has an appreciation of how the interrelationship between male and female factors influences their chances of conceiving.

In some cases, one or both individuals have a borderline problem resulting in subfertility; in other cases, both partners have infertility problems; and, in still other cases, the shared problem is one that relates to coital technique and can be helped by education and counseling rather than by medical intervention.

Couples with shared infertility find themselves preoccupied, as are their physicians, with what infertility problem to tackle first as away of maximizing one person's fertility before turning attention to the other partner's condition.

The emotional impact of the medical decision-making process is to cause both partners to be preoccupied with their own bodies and their own emotions, often not having enough energy to share with their mates. Thus, the couple with shared infertility may find themselves unable to meet their emotional needs within the relationship, needing as well to elicit support from others: family, friends, support groups, and counselors. What the couple needs is emotional replenishment of the energy they are expending on the concerns about their infertility; in addition, rather than needing to be knowledgeable about the medical condition of one partner alone, this couple needs to be knowledgeable about a broader range of information and its ramifications for timing of treatments, shifting medical priorities, and side effects of any treatments on one or both partners. Careful information sharing by physicians can enable the couple to have some sense of mastery over their shared condition which, in turn, can contribute to their emotional energy as a couple.

Idiopathic (Unexplained) Infertility

The couple that receives a diagnosis of unexplained infertility carries a unique emotional burden. They are plunged into a psychological limbo in which neither they nor their physicians know what more to do to enhance their chances of becoming birth parents. For some of these couples the diagnosis of idiopathic infertility will be the beginning of a series of visits to infertility specialists; for others it will represent the beginning of the mourning process in which they experience denial, anger, bargaining and grief, without being able to move into the final stage of acceptance. Essentially the couple feels helpless and out of control of their life plans to have a baby, and with medical professionals also baffled as to the cause of their infertility, the couple enters what is often a lengthy period of chronic mourning.

Long Term Consequences of Infertility for the Couple

Inability to Conceive. Each couple will face unique long-term consequences of their infertility, depending upon the conditions contributing to their infertility and the resolution they find as they confront their inability to have a birthchild. Couples who have been unable to conceive will need to come to terms with the specific losses represented by their infertility. Grieving these losses, although most intense in the months immediately following the diagnosis, may continue to be an issue from time to time as they face their loss of control over life hopes. For some couples who choose to exert control by pursuing adoption, artificial insemination, or invitro fertilization, the pain of their infertility may recede into the background as they put energy into new options. On the other hand, all of these options involve waiting periods, feelings of being evaluated, and chances of not succeeding, and in that sense the raw feelings aroused by infertility may still be very much in the forefront until the couple holds a baby in their arms.

Pregnancy Loss. For couples whose infertility is caused by their inability to carry a pregnancy to term, the issues are more complex. The couple knows that they can conceive, yet efforts at conception have brought them heartbreak as they have experienced miscarriages, ectopic pregnancies and stillbirths. The level of attachment that the couple allow themselves during a pregnancy will influence the extent to which they feel a sense of loss, and their feelings about their losses will, in turn, influence their willingness to undertake another pregnancy. It is common for couples to have difficulty investing emotionally in a pregnancy until after it passes the week at which the earlier pregnancy was lost (Friedman and Gradstein, 1982). In the case of a miscarriage the loss is primarily an emotional one, as the couple questions whether they will ever be able to have a healthy pregnancy. When an ectopic pregnancy occurs, there are the more concrete fears of risks to the woman's life and of the possibility that one of her tubes may burst or need to be removed, thereby impairing future fertility. When a couple has experienced the tragedy of a stillbirth, there is both the wish to have a healthy baby and the fear that their reproductive capabilities are fragile and that a future pregnancy, too, could be lost. So couples who have experienced a pregnancy loss are, foremost, highly aware of their reproductive fragility, and subsequently both hopeful and hesitant at the prospect of achieving another pregnancy. It is important that the couple be helped to mourn the losses associated with the lost pregnancy, so that they can invest in a subsequent pregnancy for its own sake and not be plagued with unresolved issues at a time that they are entitled to feel more hopeful (Shapiro, 1986).

Adoption. Couples who are unable to have birth children or who have unexplained infertility are faced with important decisions to make about enlarging their families. Adoption is an option selected by many couples, although with this choice comes the awareness that there will be an agency evaluation of the couple, that there is likely to be a long wait, and that the availability of healthy white infants is small, necessitating that the couple confront their feelings about adopting a child from another country, a child with special needs, an older child or a sibling group. This process is difficult for many couples who recognize that birth parents never need to be under agency scrutiny and do not need to confront some of the other issues associated with agency adoption (Ginsburg, 1984). Once an adoptive placement has been made, it is common for the couple to feel as though they must be perfect parents to this precious child; some adoptive parents find it hard to complain about their children (Ginsburg, 1984). On a long term basis, adoptive parents must confront whether or how or when to tell their child that he or she is adopted, and many parents are apprehensive about how a child will react to this information. Parents may also have some concerns about their adoptive child's wish to search for the birth parents, now that some agencies make information of this kind more easily available than in past grenerations. Shapiro and Seeber (1983) caution that adoptive parents with a history of infertility may face special issues when their children reach puberty and need to express their own sexuality and to learn about issues of sexual responsibility, birth control and sexual health. To the extent that this period of their adolescent's life causes the adoptive parents to reconfront some old issues in their own lives, the struggle of infertility can resurface in new ways.

Artificial Insemination. The couple found to be eligible for artificial insemination must deal with their feelings about achieving a pregnancy in a non-coital way. The clinicity of the insemination experience can be unsettling for couples, although some physicians encourage mutual involvement by asking the male to carry the semen to the person who will perform the insemination or by encouraging the couple to partake of some wine or champagne after the insemination has been accomplished. Couples who are participating in artificial insemination with the husband's sperm (AIH) face the pressures of having the male producing a specimen while the woman waits to be inseminated. It is not uncommon for the male to be unable to provide the specimen, as the anxiety attached to his role in the procedure renders him temporarily impotent. The woman is often concerned that she may not be ovulating on the day of the insemination, in spite of efforts to read home ovulation kits accurately. Many infertility clinics do not do inseminations on weekends, which can cause many couples to feel frustrated that they have missed a potential insemination because of the rigidity of the clinic's schedule.

For couples in which the male is sterile or with a very low sperm count, or when the male is fertile with serious risk of passing on congenital disease to genetic offspring, the choice is usually to use donor sperm. Couples choosing artificial insemination by donor (AID) face all the issues of couples undergoing AIH, as well as some unique issues. The Roman Catholic Church and Orthodox Judaism forbid its use; some couples have concerns about the female carrying another man's baby; the couple must grapple with whether or not they will share news about the insemination and, if so, with whom; the couple may be concerned about health problems of the donor and, more abstractly, they may wonder whether their capacity for emotional attachment to a child conceived with donor sperm will be any different than to a child that shares both of their genes.

Invitro Fertilization. For couples who select invitro fertilitzation as a method of pursuing their quest for a birthchild, a number of issues are present. First, the couple must be prepared to accept the relatively low success rate that most clinics offer (around 20%); they must be prepared to cover the costs of the invitro program, few of which are reimbursable by insurance; they must be accepting of the medication prescribed for the woman; they must be able to travel to the invitro clinic they have selected and to bear the expenses associated with absence from work, travel, and hotel stays for the male; and they must confront the immense anxiety they will face each month after they wait to see whether the fertilization has been successful. Ironically, the couple must also be prepared for the possibility of multiple births, with both the risks and potential joys of more than one baby. Finally, they will need to accept that if a pregnancy is achieved, it may be a highly stressful time emotionally (Shapiro, 1986). The couple must ultimately decide how open to be about the method by which they have become pregnant and, if a healthy baby is born, they will need to discuss whether or how and when to tell their child of his or her special way of being conceived. The couple may ultimately explore whether to have a subsequent invitro fertilization in their efforts to enlarge their family further, and at this time they are likely, once again, to be thrown back into some of the emotional issues confronted at the time of their initial invitro experience.

Childfree Living. Some couples, confronted with the rather narrow options by which they can enlarge their families, make the conscious choice to live their lives without children, perhaps deciding to channel their energies into work, into pleasure, or into substitute nurturing experiences such as volunteer work, creative endeavors or philanthropic efforts. In spite of the conscious decision not to add children to their family, the childfree couple may find that there are times they have some regrets at not having children. Mazor (1984) reports that concerns of generational identity are common. Many individuals express their concern about forever remaining the child of their parents, never fully achieving adult status. Some talk about feeling "old," about being confronted prematurely with a sense of their own mortality. They worry about being the end of the genetic line. Leitko and Greil suggest that childlessness disappears as a source of emotional distress during mid-life, not to appear again as a distinct deprivation until the late elderly years, and then as a resource deficit rather than as part of an identity crisis.

Often the times that are most vulnerable to self doubts occur around life milestones: retirement, menopause, or developments in the lives of family and friends, particularly those with children. Many couples fear the isolation and loneliness of growing old alone, and from time to time they may wonder whether they will be able to handle the process of aging without an adult child to support them and offer company and, perhaps, grandchildren. In fact, as friends of the childfree couple are rejoicing in births of grandchildren and the attention and gifts they can offer this new generation, the infertile couple may find that, once again, they feel the old social isolation emerging in their lives.

The long term consequences of infertility are universal in some ways for all couples in spite of the unique issues detailed above. For most couples, there is a level of grief that must be experienced regarding the disappointment in their reproductive functions, and mourning for the birth children they had hoped to have together. There will be feelings of social isolation when in the company of people sharing experiences of pregnancy, childbirth and breastfeeding. There may be difficult issues with parents and in-laws who are uncomfortable with the route the couple has chosen in resolving their infertility. And there may be nagging doubts by parents who have chosen adoption or AID that any problems their children have experienced would not have occurred had they couple conceived their own genetic children.

The Impact of Infertility on the Individual's (Couple's) Social and Work Relationships

The impact of infertility on social and work relationships is dependent upon a range of factors. Since infertility often is not openly discussed, and since many friends and co-workers who learn about a couple's infertility are either awkward or insensitive in their comments, it is common for a couple to begin to feel socially isolated from other fertile people.

This social isolation may extend to complete strangers, as the couple find themselves avoiding any contact with pregnant women, families with infants and small children, maternity shops, toy stores, and other reminders of the joys that they want but cannot have. Within their extended families, it is common to find sources of friction as adult siblings may be easily achieving pregnancies and drawing familial attention to new babies and away from the sadness of the infertile couple (Mazor, 1984). Parents and in-laws may give well-meaning but inappropriate advice, which the couple construes as a message to "try harder," when they believe that they have exhausted all of the available forms of medical help. Families are sometimes unable to understand the infertile couple's wish to avoid painful events, such as christenings, baby showers, children's birthdays, and celebrations over the announcement of a relative's pregnancy. The isolation and misunderstanding of familiy and friends serves to increase the couple's sense of defectiveness at a time that they most need support and acceptance.

Among fertile friends the couple may also sense a lack of support and a feeling of isolation as social talk turns to topics related to pregnancy and childrearing or as social gatherings inevitably include pregnant women, infants and small children. These reminders of their shattered hopes and dreams are extremely painful for many infertile people and, although they may choose to avoid their fertile friends altogether, what they receive in exchange is a feeling of being different and alone in their grief. Conversely, some infertile individuals make efforts to increase their level of contact with children and young people, in part as a way of satisfying their wish to nurture and in part to make up for the disappointment they feel in their personal life.

One source of comfort for some infertile couples is the opportunity to meet and share information with other infertile couples. Sometimes this happens informally or on other occasions the availability of a nearby chapter of RESOLVE may facilitate contact with other infertile individuals. RESOLVE, a national organization providing information and support for infertile individuals, has chapters in over forty cities in the United States (Menning, 1984). Couples find that contact with other infertile people allows them to be open about their emotional pain and to feel accepted and valued by others who, like them, are struggling with the impact of their infertility.

Work relationships, too, are affected by a couple's infertility. Many individuals complain that they are unable to concentrate on their work as the emotional sadness they feel threatens to overwhelm them in the workplace. In interviews with thirteen infertile couples, Leitko and Greil report that involuntary childlessness increases worry about work, especially for men. Male interview respondents claimed to be distracted from their work by conflicts and pressures at home revolving around childlessness, infertility treatment and adoption. Others complained about the expense of treatment and adoption relative to their earnings. Still others noted that having to take time off for treatment for themselves or their wives could hurt their job performance or bring to the attention of their co-workers a physical problem which they would as soon "pass" as not having. Just as occurs in relationships with family and friends, the sense of social isolation extends to the workplace as well.

Listening to co-workers exchanging complaints of everyday problems can be very irritating to the infertile person who views these complaints as petty in comparison to the emotional pain of infertility. There are concrete irritants as well, since many individuals must take time away from work for doctors' appointments, some of which are miles away and some of which involve procedures lasting for days or weeks at a time. For couples who are trying to conceive, there remains the pressure to have intercourse at the time the woman is ovulating, which may conflict with a scheduled business trip. After a period of time of grappling with their infertility, many individuals reorganize their perspective on life so that work and professional concerns no longer are paramount and do not consume the psychological energy they once did. On the other hand, some infertile individuals find that their work serves as a cushion against the pain of their infertility and that, even if they cannot be productive in the sense of bearing a child, they are capable of being productive in other spheres of their worklives. However, Leitko and Greil report that although women without children are more likely to be employed, employment is not likely to reduce emotional distress due to involuntary childlessness. In some cases, individuals who are working in occupations with pregnant women, infants or children may find that they need to change their employment in an effort not to face reminders of their pain on a day-to-day basis.

In both personal and workplace relationships, the infertile individual is likely to confront a range of pressures and supports. The crucial ability to draw upon appropriate resources without being overwhelmed by the pressures is a challenge faced by infertile people and the helping professionals who support them in their emotional struggle with infertility.

PSYCHOLOGICAL EFFECTS OF DIAGNOSIS AND TREATMENT OF INFERTILITY

The Diagnostic Process

The Female

Since females are accustomed to receiving routine reproductive health care, it is unlikely that they initially feel threatened as they mention to their gynecologist the concern that they have a fertility problem. Their past familiarity with pelvic exams, with PAP smears, with breast exams and with other measures taken in the interest of their reproductive health enables most women to tolerate some of the initial procedures of an infertility workup without undue psychological difficulty, although the procedures themselves may be uncomfortable. However, as the effort to reach a diagnosis requires more tests, additional expenses and, perhaps, hospitalization, the woman's anxiety is likely to build. She may express the fear of being defective and may harbor the fear that she is not deserving of having a child (Mazor, 1984). Since the diagnostic process involves a range of procedures, the woman is likely to feel probed and manipulated physically, and psychologically she is likely to feel the stress associated with revealing intimate details of her sexual life, with charting her basal body temperature daily, and with having intercourse on a schedule that coincides with ovulation. Some women feel a sense of stress when they ask their male partners to participate in the diagnostic procedure, especially if the desire to have children is held strongly by the female and not so strongly by the male.

A diagnostic workup can continue for months and sometimes years, and the length of time the couple must spend in this process can be highly anxiety provoking. The woman feels anger and sadness each month as the beginning of her period indicates that, once again, she is not pregnant; the couple faces decisions about the risks and costs and intrusiveness of each new procedure and, if the woman is in her thirties or forties, she feels a strong pressure to reach a diagnosis, thereby not wasting precious months in her quest to achieve a pregnancy.

The Male

Males are less accustomed than females to seek routine medical care for their reproductive health, so when the prospect arises of seeing a physician, many males feel highly apprehensive. This apprehension is often exacerbated by the need to produce a semen sample by masturbation, a process that may arouse feelings of guilt, inadequacy and anxiety in the male. A semen analysis is an important diagnostic procedure in evaluating male infertility, and several samples may be needed during the course of several months, depending upon the findings.

Since many males attach feelings of self worth and virility to the outcome of the semen analysis, the results can have an impact on the male's self esteem and his general feelings of adequacy. Menning (1977) asserts that the process of being "counted" and scored can be threatening to even the most secure male ego. One diagnostic procedure in particular can be highly stressful for males. The post coital test involves a couple having intercourse one or two days prior to ovulation, and then visiting their physician within a few hours of intercourse so that the woman's cervical mucus can be examined to determine how sperm interact with the vaginal and cervical environment of the woman. With the doctor's appointment looming, the male is truly in a situation of needing to perform on command, and the tension surrounding this may cause the male to experience temporary impotence. The same reaction may occur when the couple has charted the woman's basal body temperature in an effort to determine the day on which she ovulates. Once again the male is in a situation of needing to have intercourse on a schedule totally unrelated to his own sexual urges. For a male who has never had an experience with temporary impotence before, the entire diagnostic workup may call into question some very basic assumptions about his virility.

The time of diagnosis is usually a difficult one for couples. After having hoped that a doctor could offer an easy solution to their inability to have a baby, the couple must ultimately confront the reality that their infertility is an issue with which they must reckon seriously. Even more difficult, it may be months before any diagnostic impression can be reached. In the doctor's office, one of three scenarios may occur: the couple may be told that they have a problem for which there is no medical cure; they may be told that they have a problem for which treatment is available; or they may be told that they have idiopathic (unexplained) infertility. The psychological response of infertile couples will differ according to which of these three diagnoses they receive.

If the couple is pursuing an initial infertility workup in their local community, it is traditional for the woman to be seen by her gynecologist and for the male to be evaluated by a urologist. Diagnostic impressions are usually offered individually to the male or to the female, leaving the partner with the task of remembering the information accurately and conveying it to his or her mate. This diagnostic division of the couple often contributes to the difficulty that the couple has in viewing infertility as a problem shared by the couple, and intensifies the likelihood that one partner will carry an inordinate feeling of guilt or blame. If the couple is being evaluated in an infertility clinic, it is very likely that both partners will have been seen by specialists in the clinic and told together of the outcome of their infertility workup. For couples that have shared the experience of diagnostic tests and ongoing feedback, sharing the burden of infertility is more possible, since both partners are informed about their own and each other's condition. Also, it is likely that the process of talking together about their infertility was initiated at the time they began to receive joint feedback, and thus they are able to serve as sources of support to one another.

The time of sharing diagnostic impressions with the couple may also be a time that the couple can most benefit from psychological support. Whatever the outcome of diagnosis, the couple has some new information to process and a pressing need to weigh future options. Couples who have been in suspense for weeks or months of diagnostic tests often need help in understanding the implications of the diagnosis for future life plans so that they can make decisions with full understanding of the available options.

The Psychological Impact of Infertility Treatment

The beginning of treatment for infertility represents both a confirmation of infertility and the hope that the problem can be cured. In both the male and in the female the psychological impact of treatment will be affected by a variety of factors: how they feel about the intrusiveness of medical treatments, what potential side effects are associated with specific treatments, how flexible their personal and work lives are to the carefully timed nature of some treatments, and what level of success they have been led to associate with the particular treatments they will be undergoing.

The Female

Treatments for the female can range from medication to surgery. Women who are apprehensive about surgery or anesthesia may find themselves highly anxious as the time for surgery approaches. The anxiety represents both their fear of the procedure itself and the hopes for future fertility that are attached to the outcome of the surgery. Some women are specifically terrified of dying during surgery yet are willing to undergo such a threatening experience if it could improve their fertility. Women who must take time away from work for the surgery and recovery period will need to deal with other issues: whom to tell and how much to tell about the reason for the surgery; how to occupy the days or weeks of recovery when the woman is not accustomed to spending her time in physical discomfort and in a way that may feel unproductive; and how to meet the expenses that are not covered by insurance coupled with workdays that are lost. The recovery period is usually a time of physical discomfort, which may add to the woman's feelings of being betrayed by her body. During the post operative period it is common for the woman's hopes for a pregnancy to rise and for her to begin to feel impatient as she and her partner await their doctor's permission to try again to conceive.

The side effects associated with specific treatments can also be a source of anxiety for the woman. Weight gain, acne, hot flashes and depression are all concomitant of various medications, contributing to the woman's feelings of having her body out of control. The drug Clomid may prolong the second half of the cycle and thus increase the hope of a pregnancy that is brutally dashed when the woman's period begins. Some fertility drugs and procedures carry with them the possibility of multiple conceptions and, although many couples would welcome twins after their period of infertility, the possibility of more than two fetuses developing is worrisome to many couples who are aware of the increased risks of miscarriages, birth defects, and complications during delivery.

The woman's flexibility to take time away from work or education for infertility treatments will also influence the way in which she views the procedures. In any case, the decision to undergo treatment represents an investment in the need to have her infertility corrected. But if she has needed to make major interruptions in her work or school life, then treatment represents a sacrifice as well. The uncertainty of the outcome can leave the woman wondering whether her decision was the "right" one, and whether the ultimate outcome will be worth having given up the continuity of other aspects of her life. The woman's sense of optimism and hopefulness is likely to be influenced strongly by the rate of success she knows to be associated with the treatment she is receiving. Most women, having experienced months or years of disappointment at their inability to conceive or to carry a pregnancy to term, will be guarded in their optimism - hoping beyond hope that this treatment will be successful, but refusing to become emotionally invested in the possibility of a healthy pregnancy.

It is not unusual for the infertility treatment to be performed at infertility clinics many miles from the couple's home. In that case, the woman may be faced with separation from family and friends at the very time they might have been most helpful in offering emotional support. Even the male partner may be unable to remain at the infertility clinic beyond a few days, as the economic strains of missing work may be more compelling than his partner's need for his physical presence. The period of waiting during recovery or during ongoing treatment procedures is often immensely stressful for the woman, who must find other sources of support as family and friends are less accessible.

The Male

Males who are faced with the prospect of treatment may have a variety of reactions. For males who never have undergone reproductive surgery before, the thought of surgical intrusion can be very threatening. For other males who have had minimal contact with physicians and hospitals, there are many dimensions to their hesitation about surgery, many of which can be alleviated by a careful explanation of what to expect, both from the hospitalization and from the surgery itself. The availability of literature about the surgery also provides the male and his partner with the opportunity to review that information and to formulate additional questions they need to ask the physician.

Males whose treatment consists of a regimen of medication do not usually have the negative side effects from the medication that females experience. Therefore, medication is not usually an unpleasant treatment procedure, although there is always a level of anxiety associated with the outcome of treatment.

For males who have treatment, the semen analysis is a recurrent diagnostic procedure they must undergo in order to determine whether the quality of their semen has changed in response to treatment. Some males view the experience of masturbating in order to provide a specimen as degrading, while others cynically associate the "specimen on command" message with the entire programmed sex experience that comes to characterize their infertility experience.

The Couple

The couple involved in infertility treatment is in a period of anxious waiting. If the couple has unexplained infertility or if both partners have problems contributing to their infertility, then it is likely that both partners will be experiencing a variety of treatments in a close time span. For these couples, that may mean that each partner is so caught up in his or her own emotional needs that there is less support to offer the other. It may also mean that the couple will need help in looking outside of their relationship for the emotional support they both need. By sharing the problem of infertility, the couple may come to have more empathy for one another and may find that they grow closer through the experience of their infertility. However, infertility is a major focus of these couples' lives, and it is often very difficult for them to think of themselves except in their roles as infertile people.

For couples who begin soon after marriage to conceive a child, the diagnosis and treatment of their infertility may represent the first crisis of their marriage. To face this crisis without a history of having weathered other emotional storms presents the newly married couple with many emotional challenges: not only must they face the threat to an important shared hope, but they also must learn quickly how to comfort one another and how to express their need for emotional support. Thus, infertility may represent the first test of the resilience of their relationship at a time when each partner is also very preoccupied with his or her individual emotional needs.

In all couples dealing with infertility treatment there is likely to be some aspect of the mourning process that is being worked on. Efforts to resolve feelings of grief rarely are synchronized between partners, which often leaves the couple feeling emotionally out of step as each individually struggles with the issues that treatment presents.

As the couple faces the diagnosis and treatment of one or both partners, it is crucial that both individuals be present as much as possible at the time that information about diagnosis and treatment is provided. It is also important that the medical specialists communicate carefully between themselves in order to arrive at a consistent message for the couple, as the couple should not need to bear the responsibility of sorting out mixed messages or asking their physicians to be sure to consult with one another. Since many infertility specialists need couples to be fully informed in order to make decisions about future treatments, it is also to the advantage of the clinic that services are aimed at the couple and that they are kept fully informed as each procedure is carried out.

Psychological Changes During Long Term Treatment For Infertility

Successful Treatment

Successful treatment often is not achieved until a couple has been seen by specialists for months or years. During that time the couple has begun to come to emotional terms with the possibility that they may never be birth parents. Once treatment results in a healthy pregnancy, many of the old emotions that sustained them during their infertile period may come to haunt them during the pregnancy.

With the realization that infertility is a serious problem, many couples begin a process of anticipatory mourning for the birthchild they fear they will never have. There is an ambivalence in this mourning, for just as they are emotionally in touch with their grief, they also are actively invested in infertility treatments that they hope will cure their infertility. Anticipatory mourning represents an emotional distancing from the initial attachment they had had to their fantasy birthchild. When a pregnancy occurs, this anticipatory mourning may not halt immediately. Shapiro (1986) reports that it is not unusual for a couple to ask for a second pregnancy test and, even when the pregnancy is confirmed, for one or both partners to feel reluctant to become emotionally invested in the pregnancy. As the pregnancy progresses, one partner may permit feelings of attachment and bonding while the other remains resolutely detached. It is not unusual for the male to be the emotionally aloof partner, both because his body is not reminding him on a daily basis of the developing fetus and also because American males often are socialized to be circumspect about displaying their emotions. There is the fear that any joy the couple may allow themselves will tempt fate; this causes some couples to decide not to share the news of their pregnancy until after the first trimester when the likelihood of a miscarriage diminishes. This period of silence deprives the couple of much needed support from significant others during an emotionally difficult time. In addition to the long term impact of anticipatory mourning, the couple carries over into the pregnancy many of the therapeutic coping mechanisms learned and practiced during months and years of their struggle with infertility. The stoicism that the woman developed as she hoped for a pregnancy month after month may cause her to bear the expectable discomforts of the first trimester of pregnancy without feeling that she is entitled to complain after succeeding in achieving this much-coveted pregnancy.

Another coping mechanism that may have been important to the couple during their period of infertility is that of distancing themselves from fertile friends who served as painful reminders of the joys of parenthood that the couple feared they would never have. The resulting social isolation and, perhaps, new friendships with infertile couples, causes the couple some social uncertainty as they wonder how to renegotiate their friendships that have been constructed to protect them from further hurt associated with their infertility. Not only will the couple need to reach out to their fertile friends again, but they also will need to be sensitive to the changes that are bound to occur in relationships with their still-infertile friends whose friendships they may still value but who will have mixed feelings of happiness and jealousy toward the newly pregnant couple.

Shapiro (1986) asserts that unique issues confront the previously infertile couple once a pregnancy is achieved. If the couple has experienced one or more pregnancy losses, there will be apprehensions associated with the early months of the pregnancy. Some couples find that they are unable to enjoy their pregnancies until they have passed the week when their earlier pregnancy loss occurred (Friedman and Gradstein, 1982). In fact the memory of their earlier loss is but one factor that prevents the couple from taking full pleasure in their newly pregnant state. Couples who have experienced a previous miscarriage are sometimes advised by their obstetrician to abstain from intercourse during the first trimester. At a time when the couple is feeling the emotional strain of a pregnancy and when they strive for closeness to allay their apprehensions, it can be doubly frustrating to be denied the intimacy that intercourse can bring. Previously infertile couples are likely to have had a history of "programmed sex," whereby a premium is placed on having intercourse during the woman's fertile period. For those couples again to be denied the spontaneity of intercourse provides one more reminder that the threat of infertility still is present despite their success in achieving a pregnancy.

The issue of amniocentesis is one which many previously infertile couples must confront during the first and second trimesters. Amniocentesis, usually performed between the fourteenth and sixteenth week after the woman's last period, is available for those couples considered at special risk of producing a baby with genetic abnormalities. This could include some previously infertile women whose pregnancy losses were attributed to genetic abnormalities or who are in an age group considered at special risk for producing children with Down Syndrome. Shapiro (1986) reports that the decision of whether or not to have amniocentesis presents special difficulties for the previously infertile couple. For couples who already have undergone many intrusive and painful procedures connected with their infertility, the thought of one more test, one more period of waiting anxiously for results, and one more time of questioning their capacity to experience success in their efforts to have a baby, may cause them to question the "worthwhileness" of the test. In addition, the risk of the procedure must be considered by the couple. Hotchner (1984) reports that there is less than a one percent chance of a miscarriage following amniocentesis; however, there is concern that women with a history of miscarriages may have a higher risk of miscarriage associated with amniocentesis. So couples find themselves in the position of weighing the "need to know" against the fear that the pregnancy could be interrupted.

As the pregnancy progresses, new issues arise for the previously infertile couple. Shapiro (1986) has found that as the baby becomes increasingly real to them, some previously infertile couples refuse to acknowledge the ambivalent feelings that the pregnancy evokes; somehow they feel unentitled to anything but joyful emotions. It is almost as though acknowledging some of the mixed or negative feelings would detract from the importance of their accomplishment and the validity of their desire for parenthood. The stoicism that the couple learned to demonstrate during their period of infertility may have served to discourage them from exploring emotions with negative overtones; as a result, many couples avoid discussing some of the concerns and adjustments that all prospective parents face, instead focussing with singularly positive thoughts on the preparations for the baby's arrival.

Although most previously infertile couples are fortunate in having uncomplicated pregnancies, the risk of problems in pregnancy is statistically higher for couples who have had previous pregnancy losses. Women experiencing complications such as spotting, cramping, contractions, and premature dilation of the cervix face tremendous strains as they are ordered to curtail their activities and, in some cases, go to bed until their obstetrician believes the pregnancy is more stable. For the couple that already has felt inadequate in their reproductive capacities, the complications of pregnancy are an intrusive reminder of previous insecurities. The frequency of visits to the woman's obstetrician are reminiscent of the past infertility investigation and treatments, and the couple's feelings of loss of control return as they once more are dependent upon the medical establishment to help them with their pregnancy. The hours in bed or carrying out restricted activities provide ample leisure time for frightening fantasies to assail the woman; her partner, on the other hand, is often so absorbed in efforts to balance employment, housework and worries about the pregnancy that he has little energy to assuage his partner's fears.

The issue of keeping in control becomes paramount for many couples in the last trimester of pregnancy. Attitudes toward medical caregivers that were shaped by earlier infertility treatments will influence the way in which the partners involve themselves in final decisions around childbirth options. Couples that perceive their physicians did not want their active participation in the infertility investigation and treatment may have internalized a passive role or may have suppressed anger at being "shut out" of an investigation so intimately tied to life hopes. This anger or passivity will very likely influence the couple's relationship with their obstetrician, in some cases the same physician who treated them for their infertility. On the other hand, for couples who are encouraged to demonstrate an active involvement in plans for labor and delivery, the last trimester provides an excellent opportunity for them to feel like full participants in a much-longed-for event. For those couples who have experienced complications during the pregnancy, the last trimester brings both hope and fear. Having sustained the pregnancy until the last trimester is a source of triumph, even though the couple is highly sensitive to the risks of the final weeks.

Unsuccessful Treatment

Unsuccessful treatment for infertility represents a profound tragedy for the couple who has invested so much hope, time, money and lifestyle adjustments in the possibility that they might one day give birth to a baby. At some point the couple, with their physicians, must acknowledge that since further treatment is not likely to be successful, the couple should end its medical quest for fertility. Some couples will move ahead toward adoption as a way of building their family, while others will choose to remain childfree and channel their nurturing capacities into other activities.

Couples for whom treatment is unsuccessful must come to terms with the many losses that their infertility represents. The loss of their dreamchild is often the most tragic one for the couple, but added to that are other losses: the loss of the role of being a birth parent, the loss of trust in their reproductive capacities and the sense of bodily betrayal that evokes, the loss of control over life plans, and the loss of feeling normal in a predominantly fertile world. These losses will need to be mourned, and the readiness to undertake this difficult emotional work differs with each individual.

Several authors (Menning, 1977; Shapiro, 1982) utilize the framework developed by Elisabeth Kubler-Ross (1969) to explain the mourning process that infertile individuals work through. In this framework, a person grappling with a loss first experiences the stage of denial, in which the full impact of the loss is not absorbed. The next stage of the process is that of anger, during which the individual feels and expresses the rage associated with the loss. The stage of bargaining often follows, in which the individual makes real or symbolic offers of good behavior, as if in an effort to delay the reality of what is a perceived punishment for unattoned bad deeds. When the period of bargaining passes, the individual enters a period of active grief in which tears, sadness and preoccupation with the lost object are a major focus. Ultimately most individuals emerge from the stage of active mourning and progress to the last stage of acceptance, in which they are able to reorder their lives around the loss they have sustained without being preoccupied with the loss. These stages are not always experienced chronologically, nor are do all individuals experience them with the same intensity. Yet an awareness of a framework in which the mourning process occurs can enable others to understand the therapeutic value of such otherwise disruptive responses to infertility as denial, anger, bargaining, and grief. The stages of the mourning process originally conceptualized by Kubler-Ross may have been partially completed as the couple anticipated the unsuccessful outcome of their treatment.

Whether experiencing anticipatory mourning, partial mourning, or fully mourning the losses that infertility has introduced into their lives, infertile people struggle with the emotions of denial, anger, bargaining, grief and acceptance. Painful as these emotions are for each individual, they are doubly painful for the couple, both partners of whom are emotionally bereft and unable to be fully supportive of the other. Also, partners rarely are struggling with the same emotions at the same time, so they may find themselves at different places emotionally as they need to rely on one another for support. In couples where one partner is actively mourning and the other is still denying the impact of the losses of infertility, there is a unique burden in that the couple itself cannot move ahead in its decisions until both partners have acknowledged and accepted the extent of their individual and shared losses.

Individuals will either use the termination of medical treatment as an opportunity to bring closure on the mourning process, or they may enter into a chronic mourning process. Whereas reaching closure is most likely to consist of raw grief and some depression that subsides over time, chronic mourning is characterized by a latent sadness that surfaces from time to time as life events remind the individual of the emptiness of life without birthchildren.

Especially for women with endometriosis, the physical pain of their condition serves as a constant reminder of the emotional anguish they endure. These women may avoid having surgery to relieve them of their pain because such surgery could reduce or impair totally their fragile chances for conceiving. Chronic mourning may also be an issue for the couple with unexplained infertility who cannot bring psychological closure on their hopes that someday they may conceive. This is also the experience of males with low sperm counts who know that, although unlikely, there still remains the possibility that they could impregnate their partners. For those infertile people, the issue of mourning is unique. They probably already have experienced the stages of acute grief without being able to achieve the final stage of acceptance, since their infertility represents more a partial loss than a final loss. Shapiro (forthcoming) reports that some couples actually say that it would be far easier at this point if a doctor could tell them that they will never give birth to a child, as this news would allow them to get on with their lives and the decisions that have been on hold for so long. For couples who have been so emotionally invested in the hopes of having a baby, the ending of medical treatment does not necessarily end their physical pain or the sense of emotional limbo as they hope that they may yet be able to experience a healthy pregnancy.

The Psychological Impact of the Cost of Infertility Treatment

The cost of infertility treatment must be considered to consist of the cost of medical procedures, the expenses related to travel to the treatment site, living expenses during the treatment period, the cost of missing work, and, in some cases, the cost of childcare for adoptive parents or parents with secondary infertility. For couples who have medical insurance, many of the initial diagnostic procedures can be fully or partially covered. However, this is often highly dependent upon the sensitivity of the physician, who must label every condition with a diagnosis in order for the patient to be eligible for reimbursement by an insurance company. Most infertility specialists and their billing clerks are highly aware of the relevant diagnostic labels, thereby helping their patients to avoid paying large sums for initial diagnostic procedures.

Individuals carrying no insurance usually have little money of their own to spend on diagnosis and treatment of infertility. Unless they qualify for Medicaid, these individuals are unlikely to be able to pursue an infertility workup beyond the most basic tests. Even for those individuals eligible for Medicaid, there is the problem of finding an infertility specialist who accepts Medicaid and, once such a physician is located, the individual will find that few elective surgical procedures are covered.

Once individuals with insurance or Medicaid have exhausted the diagnostic process and are ready to proceed to treatment efforts, they find that many surgical procedures are covered minimally or not at all beyond their own financial resources. Most couples are at this point psychologically fragile, as they have come to recognize that they have a very real fertility problem that may or may not respond to treatment. When they must next confront the financial burden that they will face in agreeing to various treatment procedures, this compounds their anxiety and, in some cases, adds to their ambivalence about entering into treatment. Some couples, once they become aware of the financial costs, must decide whether to risk their savings on treatment or to invest that money in adoption proceedings. Since eligibility for agency adoption is influenced by the couple's age, older couples feel a particular conflict about needing to decide between treatment and adoption.

Some doctors find that patients bring their anger about financial costs into discussions with the physician and other medical staff. Other physicians relate that, for economic reasons, many patients decide to stop treatment for awhile until they can once again afford to pay the mounting bills. For couples in their late thirties and early forties this presents an especially painful dilemma, as they feel that each month passing by is a crucial month to maximize their treatment options.

Many individuals stoically contend with financial pressures and, at the very time that they would otherwise seek psychological counseling, defer this as a luxury, preferring instead to pay whatever money they have for medical treatment rather than the psychological support that they also very much need.

Integrating Psychological and Medical Treatment for Infertility

There are several models used by infertility clinics to meet the psychological needs of their patients. A common practice is to hire staff with expertise in the physiological problems of infertility, hoping that these professionals also will be understanding and sensitive to the emotional stresses associated with infertility diagnosis and treatment. In a setting with this arrangement, the patient carries the responsibility of expressing emotional needs. Most expressions of need are oriented to specific procedures, rather than to the feelings of generalized anxiety and tension that the patient may experience in his or her life away from the clinic setting.

A slightly more responsive model involves having the clinic utilize a consultant on a case-by-case basis. The consultant would be alerted by medical staff when an individual or a couple evidenced extreme emotional distress, particularly if it interfered with the successful outcome of treatment. Although this model utilizes a professional trained in counseling, the way of gaining access to this person's services is to demonstrate inadequate coping skills or an extremely high level of tension or anxiety. Since the consultant is made available only after the patient is clearly overwhelmed, the degree of emotional distress may require long term counseling to work through some dysfunctional means of coping that have become entrenched in the patient's lifestyle.

A yet more responsive model is offered by those clinics that have a professional counselor on their staff. Usually this person's responsibilities involve meeting with each individual or couple on their first visit to orient them to the clinic services. At this time the professional also may make an effort to alert patients to the expectable emotional strains of the diagnosis and treatment experience. Community resources are often mentioned at this time, particularly any nearby chapters of RESOLVE or any support groups of infertile people who meet on a regular basis. Some professionals encourage patients to join the national RESOLVE organization as a way of decreasing feelings of isolation and gaining access to information about their medical conditions and emotional needs. Although the professional encourages patients to set up an appointment if they have any emotional needs that they would like to explore, patients rarely pursue this option. It is thought that there are several reasons for patient reluctance to initiate a counseling relationship. One reason has to do with the timing of the offer: since patients meet with the counseling professional on their first visit to the clinic, they are feeling highly anxious about the outcome of their meetings with medical professionals. This anxiety may cause them to focus in the interview on information that is concerned with medical procedures and expectations, rather than giving any priority to their present or future emotional needs. Also, since they have not yet begun a long term investigation of their infertility, patients may discount the professional's mention of the emotional stresses that infertile patients commonly experience in the process of diagnosis or treatment. On the first visit most patients are highly hopeful that they will meet with success in resolving their infertility and do not want to contemplate the possibility of emotional disappointment and stress. This model, which takes something of a preventive approach to the treatment of infertile patients' emotional needs, reaches out without necessarily being able to follow through.

The following model, while not currently in use by any of the infertility clinics contacted in this study, merits serious consideration by any clinic that wants to be responsive on an ongoing basis to its patients' emotional needs throughout the diagnosis and treatment process. In this model, each individual or couple would meet with the counseling professional on the first visit, both as a way of learning what to expect from the clinic and also to explore the emotional responses thus far to their infertility experience. The professional could use that discussion as a basis for expressing his/her acceptance of emotional stress as an expectable component of the infertility experience. The professional would then offer ways in which s/he attempts to minimize the emotional distress for clinic patients, including regular check-ins with all patients, short term counseling for particularly stressful times, referrals to community professionals for long term counseling, and the invitation to join a support group of infertile patients conducted by the professional in the clinic. Although the professional might not mention it at an initial meeting, his/her services also would include daily visits to the surgical ward of the hospital, both to discuss patient apprehensions prior to surgery and to offer support and advocacy during a hospital stay. This model is both preventive and responsive in its approach to the emotional needs of infertility patients. It acknowledges that infertility can be expected to produce emotional stress and provides a variety of options for patients to use in meeting their emotional needs. In addition, the efforts of the professional to check in with patients on a periodic basis relieves the patient of the responsibility of seeking out the professional, although patients who choose to initiate contact can do so. Recognition by the professional of the emotional stress of the hospital experience enables him/her to be readily available at a time when support may be very much needed and appreciated. In short, this model represents a dynamic interplay between the professional's awareness of potential needs of patients and the encouragement that patients are helped to feel around utilizing the range of services provided by the professional.

Counseling Options Available for Infertile People

The emotional stress of infertility is compounded by the lack of social institutions that legitimize and permit the mourning that infertile individuals need to do. Rituals such as wakes, sitting shiva and funerals do not exist to help infertile people put to rest the attachment they have developed to their dreamchild; instead they experience the reactions of a predominantly fertile world unable to comprehend their pain. In an effort to come to terms with the losses represented by their infertility, many infertile individuals and couples seek psychological support. Since the time of diagnosis and treatment is especially stressful for many individuals, it is expectable that the infertility clinic is one place they may inquire about counseling services.

Even if a professional therapist is associated with the clinic in which an infertile person is a patient, this therapist may not be utilized. There are a variety of reasons for nonutilization of clinic therapists. The clinic may be a long distance from the patient's home, which will make many patients anxious to proceed with the medical aspects of treatment, seeing psychological therapy as something that would be too time consuming at a time when efficiency takes priority over personal needs; some patients who already feel medically vulnerable do not want to open themselves to acknowledging their emotional vulnerability as well, and thus avoid seeking out psychological services; at many clinics the patient's medical appointments will be timed according to a variety of factors such as times of ovulation, availability of clinic staff to carry out certain procedures, and the patient's own schedule. For a patient whose need for ongoing counseling may not coincide with medical appointments at the clinic, there will be feelings of dissatisfaction as unmet psychological needs must await the next scheduled clinic appointment. This is particularly a problem when lengthy geographical distances are involved. Lastly, it is possible that a patient will acknowledge the need for psychological services but feels unable to relate comfortably to the professional therapist on staff at the infertility clinic.

For infertile people who do not receive psychological counseling at their infertility clinic, there are a variety of options that they may pursue. County mental health clinics and private family counseling agencies often have therapists on their staff who can relate to many of the issues that infertile individuals and couples face: loss, crisis, lowered self esteem, identity issues and relationship issues. These agencies tend to have sliding fee scales, so that the couple who must bear the financial burden of their infertility treatment may be able to negotiate a manageable fee for counseling. The disadvantage of agency counseling is that very few therapists (with the notable exception of adoption workers) are at all familiar with infertility as a life crisis and may be uncertain how to approach this issue with couples and individuals. In addition, since medical diagnosis and treatment cause so much of the stress that infertile people experience, a therapist who is unfamiliar with the medical aspects of infertility may depend inordinately on the infertile client for information about the significance of certain tests and procedures. Whereas a therapist associated with an infertility clinic can work as a team member with many of the medical professionals, even serving as an advocate if the patient's needs are not being met, a community therapist would have little opportunity to communicate with the members of the infertility team involved in the overall treatment program.

Some infertile individuals seek out the services of support groups in their communities. Many local chapters of RESOLVE have support groups and, even if a formal support group is lacking, the ongoing informational programs and association with other infertile people on a regular basis help to reduce the feelings of isolation so common among infertile people. In addition to support groups offered through RESOLVE chapters, some communities have other support groups that are relevant to infertile people (support groups for people who have experienced miscarriages, stillbirths, chronic illnesses or more general groups, such as those that focus on decision making, personal relationships and future life goals). Beverly Freeman, executive director of National RESOLVE postulates that infertile people who connect with support groups of other infertile people usually are able to satisfy their need for psychological support without seeking therapy on a more formal basis.

In many communities there are telephone counseling services for troubled people who are reluctant to be more public about seeking help. Many RESOLVE chapters have one or two volunteer telephone counselors who are prepared to offer brief telephone counseling and, if desired, refer the caller to a competent community professional with whom they might discuss their needs in more detail. Other community hotlines, while not staffed with counselors who have any expertise in infertility, may still offer callers the opportunity to explore their feelings of distress and, in doing so, to feel accepted and less isolated.

In addition to counseling available through public and private agencies, many therapists have private practices in their communities. The costs associated with private therapy usually are higher than the costs of agency services, but individuals may be able to be seen more promptly by a private therapist, as many agencies have waiting lists. Also, when seeking agency services, the infertile person has less choice, if any, with regard to the identity of the therapist with whom he or she will work, whereas this choice is far more available when seeking a specific therapist in private practice. Fees of therapists in private practice often are able to be reimbursed through health insurance coverage.

Many couples seek out a religious leader as a counselor during their efforts to come to terms with their infertility. Relatively few clergy are knowledgeable about infertility, although many are able to relate to the feelings of loss and, sometimes, betrayal of faith, that individuals are trying to resolve. Religious leaders also may be particularly helpful in clarifying their religion's stance on such topics as artificial insemination by donor, a practice that is forbidden by some religions.

Although infertile individuals have a variety of options available if they seek counseling for their infertility outside of the clinic setting, they will need to be aware that few therapists are very knowledgeable about infertility and the kinds of issues that it precipitates for individuals and couples. In addition, therapists and counselors outside of the clinic setting will have little or no opportunity to communicate with members of the medical team providing infertility treatment and, thus, will be unable to work in a way that views medical and psychological treatments as complementary and interrelated.

The Lifelong Legacy of Infertility

Issues that are Resolved with the Birth of a Child

The birth of a healthy child to a previously infertile couple provides a tremendous sense of fulfillment. The couple now knows that it will have one child to cherish, although there may be nagging doubts about the efforts necessary to achieve future pregnancies. The anticipatory mourning that occurred during infertility treatment disappears as the couple emotionally reorients their lives to the needs of their newborn infant. Self image of both parents tends to improve once they are able to invest their energies in the parenting role and to feel normal once again in a predominantly fertile world. In general the couple has less need to shelter and protect themselves from the previously painful reminders of their childless state: they can now shop for toys, attend baby showers, see pregnant women and infants, and rejoin their friends with children in social relationships that may have been painful during their period of infertility.

The birth of a child may end some of the couple's feelings of dissatisfaction about their relationship, especially if these feelings were rooted in the mourning process, which has now been replaced by a joyful emotional investment in parenting. However, if some of the couple's difficulties were present prior to their infertility struggle or if the emotional estrangement of the infertility period was profound, there may continue to be difficulties in the relationship that are not resolved by the birth of a child. It is important to recognize that becoming parents for the first time represents a developmental crisis for the couple (Scherz, 1971; Rhodes, 1977), and there will be stressors associated with their enlarged family, as well as the long-awaited joys and satisfactions.

Issues that Continue Despite the Successful Outcome of Infertility Treatment

The Couple's Sexual Relationship. Certain issues seem fairly universal for parents with a history of infertility. One of these issues has to do with the couple's ongoing sexual relationship that for so long may have been influenced by the woman's ovulation, as the couple focused their efforts on procreation at the expense of sexual spontaneity and pleasure. Some couples move easily back into pleasurable sexual experiences, but many must work hard to overcome the months and years of programmed sex as they strive to regain the sexual pleasure that characterized their relationship before infertility became an issue. Another issue that couples face is birth control. For couples who have tried steadfastly to conceive, the prospect of practicing birth control feels strangely ironic: on the one hand, the couple wants to exercise control either in terms of spacing future children or in terms of limiting the size of their family. On the other hand, after having tried for so long to conceive, many couples feel that using birth control at all discounts their efforts to overcome their previous infertility. For couples who can accept the practice of using birth control, there may remain a concern that their method of contraception may fail and leave them with an unintended pregnancy. The apprehension felt by one or both partners at the prospect of an unplanned pregnancy can wreak havoc on sexual relations, as well as contributing to the feeling of being out of control reproductively, although in a far different way than experienced during their infertile period.

The Impact of Infertility on Parenting. The early years as parents often are spent trying to balance the idealism of wanting children with the reality of having them. Some couples respond by having unrealistically high expectations of themselves as parents. Such parents are unnecessarily hard on themselves for problems in childrearing, somehow believing that every problem could have had a more beneficial outcome if only they had "tried harder," "known more," or "been better." Not only are such expectations unnecessarily harsh for the parents, but they also place a burden upon the children who receive the implicit message that they are a reflection of their parents' adequacy or inadequacy. The opposite aspect of expecting too much from one's children is not expecting enough, and this can be manifested in terms of parental overindulgence.

Perhaps one of the most unspeakable fears that haunts the parent with a history of infertility is the fear of losing the child who is so precious. It is not uncommon for parents with such fears to be highly protective of their children, acutely aware of dangers and risks. Another consequence for parents who fear losing a much-loved child is the need to conceive or adopt another child soon. In the case of birth parents, this may represent the need to prove their continuing fertility; for adoptive parents there may be a very real pressure to begin adoption efforts promptly, given the uncertain waits associated with both public and private adoption.

When the children of infertile parents reach adolescence, a whole new set of challenges can occur. For some parents, their period of infertility may have left them feeling uncertain about their own sexuality and they may experience more than the expected awkwardness in discussing sexual issues with their adolescents. The topics of birth control and abortion are especially emotion laden for parents with a history of infertility. Efforts of adolescents to achieve autonomy may raise a special challenge for previously infertile parents. When the adolescent begins to move away from the family, either geographically or emotionally, parents may have a particularly difficult time letting go. For parents who have invested so much in that role, less involvement with one's offspring may evoke a resurgence of the emptiness that characterized their period of infertility. The efforts of young people to differentiate their identities tends in many families to coincide with the onset of menopause for the mother. The feeling of constant transition may revive feelings of loss of control and result in parents holding tightly to their children at the very time the children need an opportunity to experiment with autonomy.

The Impact of Menopause. The cessation of menstruation presents adjustments for all women. Previously infertile women may feel a psychological let down as they contrast the end of opportunity for bearing children with the earlier determination and tenacity they displayed during their efforts to overcome their infertility. Indeed, the revival of preoccupation with one's reproductive health can itself be an unwelcome reminder of the earlier infertile times.

Interacting With Adult Children. Shapiro (forthcoming) contends that pangs of emotion stemming from infertility sometimes return when children marry and contemplate having children. Parents may feel tempted to encourage their sons and daughters to have children as soon as possible. In addition to ascertaining that their children are fertile, parents may also want to save their children the pain of infertility brought on by delaying efforts at childbearing until after the peak fertile years. Parents who had difficulty letting go of their own children may feel the need for grandchildren as a way of strengthening the ties with their adult children. And, because individuals with a history of infertility are typically older when they first become parents, they may want the pleasure of enjoying grandchildren while they are still energetic and healthy.

It is understandable for individuals to feel resentment that their previous infertility continues for many years to haunt them in unanticipated ways. The fear that some people have is that their infertility will prevent them from feeling a sense of control over their lives. It is, in fact, a significant experience in the individual's life and deserves to be reckoned with. Previously infertile people should be encouraged to discuss the sense of mastery they have achieved over their infertility; they may be able to anticipate times in the future when their infertility may once again be an issue; and they can be encouraged to be insightful about their original struggle as a way of gaining a sense of ongoing learning about themselves and the impact of infertility upon their lives.

THE PSYCHOLOGICAL CAUSES OF INFERTILITY

Two decades ago psychogenic factors were thought to be causative in about 30 to 40 percent of all infertile couples (Mazor, 1984). Leitko and Greil report that the majority of studies linking infertility to emotional distress have worked from the assumption that emotional distress causes infertility (Bell, 1981; Noyes and Chapnick, 1964). Higher than normal levels of anxiety, stress, and depression, especially among infertile couples with unexplained infertility, commonly are taken as evidence in support of this assumption (Bell, 1981). This research has been criticized on methodological grounds for failing to establish evidence of a causal sequence in which emotional distress precedes the onset of infertility (Noyes and Chapnick, 1964). Some researchers, in fact, now believe that the sequence is actually reversed, and that the emotional distress being measured is evidence of emotional distress in response to infertility rather than emotional problems causing infertility. This interpretation supports the reports of clinicians, such as Menning (1982), Bresnick (1981), and Mazor (1984) of an emotional "life crisis" following the realization of infertility problems.

With the advent of sophisticated diagnostic techniques and a better understanding of reproductive physiology, a diagnosis can now be established for over 90 percent of infertile couples; through treatment, about half of these can be helped to achieve a pregnancy (Mazor, 1984; Menning, 1977). Thompson (1984) reports that infertility can be attributed totally or partially to male causes in 40 percent of cases. Women have the infertility problem in another 40 percent of the cases and the couple share a problem in the remaining 20 percent of cases (Menning, 1977). In the female, approximately 30 percent of infertility is due to tubal causes, 20 percent to ovarian causes, and 15 percent to cervical causes (Thompson, 1984). The 10 percent of couples having undiagnosed infertility are often targeted as those whose problem could be attributed to psychogenic causes, but it is also plausible that the current medical technology is not sufficiently refined to detect a physiological problem. Mazor (1984) asserts that the influence of higher nervous system centers on human reproduction is poorly understood; stress may indeed play a role in ovulation and spermatogenesis, but no evidence exists that the stress is specific. Many stress-related problems are short term in duration and so do not account for the unexplained infertility of couples who have been trying for years to conceive.

SEXUAL DYSFUNCTION AND ITS IMPACT ON ACHIEVING CONCEPTION

Loss of Libido

Loss of libido is experienced by many infertile couples in the course of an infertility workup. Some infertility specialists note that a loss of libido seems to be associated with the initiation of diagnosis, as the couple feels its sex life to be open to examination and alteration by various medical professionals. The couple who once had sexual relations spontaneously may find it harder and harder to perform "on command" for post coital tests and at times of the female's ovulation. Some physicians note that couples seeking an understanding of their infertility reveal that loss of libido is a factor. However, rarely do physicians find than this is due directly to psychological factors. Physical exhaustion, substance abuse, use of hypertensive drugs and of tranquilizers often are found to result in loss of libido. A loss of libido usually has as a consequence infrequent intercourse, with reduction in the likelihood of intercourse at a woman's most fertile time of the month. Infertility specialists treat loss of libido according to the cause. Information and education can enable a couple to weigh the importance of altering their lifestyles so as to minimize exhaustion and to maximize the timing of intercourse with ovulation. Although physicians often find their advice ignored, they counsel patients who have alcohol and drug abuse problems to terminate their use of these substances, both because of their effect on libido and also because of their effect on a developing fetus, should the woman become pregnant. In most cases, other medications can be altered so that their effect on libido is minimized.

Conditions that Result in Sperm Deposition Failure

Sperm deposition failure can be a contributing factor in a couple's infertility, although the majority of infertility specialists contacted in this study did not see this as a problem with a psychological cause. Rather, they cited a number of physiological causes for sperm deposition failure. In cases of impotence, causes such as diabetes, diseases of the nervous system, vascular disease, pituitary tumors, substance abuse and smoking in some men may contribute to the problem. Both premature ejaculation and inhibition of orgasm in males were considered rare presenting problems, in part because infertility specialists speculate that patients would have received treatment for such conditions prior to coming to an infertility clinic. All physicians contacted indicated sex therapy as the treatment of choice for these ejaculatory difficulties. The female problem of vaginismus also is rarely encountered in infertility clinics, and when it is physicians find that teaching muscular relaxation to a woman with this problem can have beneficial results in many cases. Referral to a sex therapist is considered an alternative for couples where relaxation efforts do not result in successful intercourse. Although psychological factors may be present in women with vaginismus, the physiological problem of endometriosis makes intercourse extremely painful for some women.

REPRODUCTIVE FAILURE AS A RESULT OF STRESS OR ANXIETY

Although amenorrhea and oligomenorrhea rarely are encountered in the infertility clinics contacted in this study, physicians indicated that its occurrence usually can be traced to physiological causes such as substance abuse, excessive exercise, severe weight loss, endocrine problems and developmental abnormalities. Likewise, anovulatory cycles, a frequent problem among infertility patients, were rarely attributed to stress by physicians but, instead, were usually found to have a physiological cause, such as cystic ovary disease or hypo or hyper function of the adrenal or thyroid glands. Freeman, Garcia and Rickels (1983) compared behavioral and emotional factors in a group of anovulatory infertile women. Conclusions in the study were that neurotic personality structure or psychopathology were not significantly greater in the treatment group than in the comparison groups.

Treatment of reproductive failure is thus offered on a medical rather than on a psychological basis for most infertility patients. The long term consequences of unsuccessful medical treatment often result in extreme stress for the infertile couple as they must face the possibility that they will be unable to conceive a child. On the other hand, the diagnosis of their problem as one with a physiological cause spares most couples the feelings of guilt and self blame they might experience if they believed that their infertility was within their psychological capacity to control.

THE PSYCHOLOGY OF INFERTILITY ASSOCIATED WITH MILITARY SERVICE

Post Traumatic Stress Disorder

Impaired Fertility

Veterans' Hospitals contacted in this survey indicated that impaired fertility is an unusual complaint among veterans being treated for PTSD. In the few cases that have occurred, impaired fertility was due to organic causes: diabetes was responsible in one case and a congenital genetic abnormality was responsible in the other case cited.

Reproductive Dysfunction

It was reported that some veterans with PTSD refer to sexual dysfunction as one of a series of issues that they are confronting. Most of these veterans present themselves with the primary problem of depression, and sexual dysfunction is perceived as secondary to the depression. It is unusual for Veterans' Hospitals to see a patient who offers sexual dysfunctioning as the presenting problem. One case was cited in which the drug therapy prescribed to treat PTSD was found to be responsible for the veteran's sexual dysfunctioning. It was also mentioned that many veterans have a fear of allowing themselves to have any strong feelings, even positive feelings, because their past experience with such feelings is associated with losing control and aggressive behavior. The inability to distinguish between strong sexual feelings and feelings of aggression or hostility cause these veterans to fear losing control and having a violent outburst; they deal with this by denying the strength of their feelings which, in turn, limits their capacity for intimacy and emotional attachment.

Other Psychological Problems That Can Result in Infertility

Disabled veterans often have poor body images which affect their desire to be intimate. Concerns over intimacy also are found in combat veterans who lost close friends in combat and who withdraw from close relationships out of the fear that they will become emotionally attached and subsequently lose the person.

Fear that exposure to Agent Orange may affect offspring does not appear to be a concern major enough to affect fertility, although the small number of veterans who raise this issue are found to be quite anxious. However, among veterans who have already borne children and who find that their children have abnormalities that the veterans believe are linked with Agent Orange, there are serious concerns about what risks future offspring may face. In the hospitals surveyed there have never been any inquiries about donor germ cells (artificial insemination by donor or ova donation).

Availability of Services and Types of Treatment Used

Most of the Veterans' Hospitals have psychiatrists, psychologists or social workers on their staff, and these professionals are called upon to counsel veterans whose concerns affect their sexual functioning. None of the hospitals contacted has a sex therapist on staff, although some expressed that such a service would be utilized if it existed. Although sexual dysfunctioning is rarely the presenting complaint of a veteran, it is a frequent problem among veterans with depression, with organic problems (such as diabetes or aging), and with difficulties in interpersonal relationships.

Referrals to nearby infertility clinics are made in those few cases where the concerns relate to infertility rather than to sexual dysfunctioning.

Appendix A

Appendix A

INSTITUTIONS PROVIDING DATA FOR THIS STUDY

Infertility Clinics and Invitro Fertilization Clinics

- Vanderbilt Invitro Clinic
- UCLA School of Medicine IVF Program
- Michael Reese - University of Chicago IVF-ET Program
- Cornell University Medical College Program of IVF
- Tulane Fertility Program
- Mid York Fertility Clinic (visit)

Veterans' Administration Medical Centers

- Bath, NY (visit)
- Atlanta, GA
- Cheyenne, WY
- Long Beach, CA
- Madison, WI

Other

- National RESOLVE
- Ferre Institute (visit)

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RELIGIOUS AND SECULAR PERSPECTIVES ABOUT INFERTILITY PREVENTION AND TREATMENT

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This essay has been prepared for and has been submitted to the Office of Technology Assessment, Congress of the United States

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PART I - INTRODUCTION

A. Emergence of the New Reproductive Technologies

Tremendous public attention has focused recently on techniques for preventing and treating infertility. This is in part due to an increasing number of couples for whom conception is problematic, and in part due to the increasing availability and success of new techniques for treating infertility (the "new reproductive technologies"). The recent attention to these techniques should not obscure the fact that many of them have been in existence for some period of time (69).

The first modern recorded successful accounts of artificial insemination include the work of Lazzaro Spallanzi (1722-1799) in female dogs and the work of Dr. John Hunter of Scotland (1728-1793) in humans. The next recorded successes come from the mid to late nineteenth century. Dr. J. Marian Sims (1813-1883) artificially impregnated six women using the sperm of their husbands. His techniques slowly spread through the western world in the late nineteenth century. Leaving aside the bizarre case of Dr. William Pancoast of Philadelphia who is alleged to have used the sperm of a young medical student to inseminate a patient without her knowledge in 1884, therapeutic donor insemination was pioneered by Dr. Robert L. Dickinson in the 1890s. Despite these early successes, these techniques were not widely employed until after World War II.

The history of in vitro fertilization is more complex because successful in vitro fertilization requires the ability to obtain without damage an ovum, to maintain the ovum extracorporeally until fertilization, to successfully fertilize it, to maintain the zygote extracorporeally until the blastocyst stage, and to prepare the uterus for a successful implantation at the right time. After much early animal work, Chang, in 1959, working on a rabbit model, proved that mammalalian eggs could be fertilized in vitro. Considerable research efforts on human in vitro fertilization go back to the work of Dr. John Rock in the 1940s. That work culminated in the first in vitro fertilizations resulting in live births in England in 1978, in Australia in 1980, and in the United States in 1981.

Finally, the history of surrogate/host motherhood can be told more briefly. In 1976, a Lebanese Muslim, Tom, with an infertile American wife, Jane, contacted a Michigan attorney, Noel Keane, to arrange to find a woman who would agree to be artificially inseminated with Tom's sperm and to bear a child to be adoped by Tom and Jane in return for a fee. The first child delivered by a surrogate mother was born in 1978. By 1983, 175 surrogate babies had been born worldwide.

B. The Many Responses by Professional Groups and/or Public Commissions

This history of the development of the new reproductive technologies is paralleled by a history of increasing moral and theological concern with their moral licitness. That concern will be documented in Part II of this report, where we discuss the views of the various religious and secular communities. It is important to note, however, that there was little attention paid to these issues by professional groups and/or by public commissions until the 1970s.

The list of statements by professional groups and by public commissions since then is very impressive. We note, in the English-speaking world, at least the following (47):

TABLE I.B

U.S.A.

Report and Conclusions of the Ethics Advisory Board of the Department of HEW (1979)

ACOG Committee Statement on Human In Vitro Fertilization and Embryo Placement (1984)

ACOG Committee Statement on Ethical Issues in Human In Vitro Fertilization and Embryo Placement (1986)

American Fertility Society Ethical Statement on In Vitro Fertilization (1984)

Ethics Committee of the American Fertility Society, "Ethical Considerations of the New Reproductive Technologies" (1986)

A.M.A Policy Statement on Artificial Insemination and In Vito Fertilization (1983)

A.M.A. Judicial Council Statement on Artificial Insemination (1984); on In Vitro Fertilization (1984)

Great Britain
Feversham Committee Report on Artificial Insemination (1960)

Report on Artificial Insemination by the Peel Commission of the BMA (1973)

Report of the RCOG Ethics Committee on IVF and Embryo Replacement (1983)

Law Society of Scotland, "Draft Submission on Government Inquiry into Human Fertilization (1983)

BMA Working Group on In Vitro Fertilization (1983)

Warnock Committee Report on Human Fertilization and Embryology (1984)

Medical Research Council "Report of Inquiry into Human Fertilization and Embryology" (1985)

DHSS, "Legislation on Human Infertility Services: A Consultation Paper" (1986)

British Commonwealth
Canada - British Columbia Royal Commission on Family Law Report on Artificial Insemination (1975)

Report of the Advisory Committee on the Storage and Utilization of Human Sperm (1981)

Law Reform Commission of Saskatchewan (1981)

SOGC Statement on In Vito Fertilization (1984)

Ontario Law Reform Commission, Report on Human Artificial Reproduction (1985)

Australia - National Health and Medical Research Council
Statement on In Vitro Fertilization (1982)

Victorian Government Committee to Consider the Social
Ethical and Legal Issues Arising from In Vito Fertilization (1983)

This list is by no means complete, even for the English-speaking world, and there are of course analogous statements in the non-English-speaking world.

It is not germane to this report to summarize in detail the recommendations of each of these reports. It is germane, however, to note the following major trends which emerge as one studies them: (1) These reports support A.I.H, A.I.D., and I.V.F. as treatments for infertility; (2) They impose guidelines on the use of these techniques. These vary from report to report. Among them are restrictions on their use to stable couples, restrictions on their use to physicians practicing in appropriate facilities, and restrictions on information to protect confidentiality. They also include provisions to insure informed consent of all parties and to clarify the legal status of children born as a result of these technologies; (3) The greatest controversy surrounds the issues of surrogacy, the treatment of non-implanted zygotes, and the use of these techniques by single women; (4) Little explicit attention is paid in any of these reports to the views of the religious and secular communities of the countries in question on these issues.

C. - Importance of Taking into Account Relevant Religious and Cultural Beliefs

There was a time in which the citizens of particular countries shared a single religious and moral world view which shaped the values, beliefs, and practices of individuals. Such societies could base their laws and social policies on that shared world view. This is not to say that they would or should use the coercive mechanism of the law to enforce all moral provisions of that world view, since some might more appropriately be disseminated rather than enforced. Still, the moral foundation of legislation and social policy in such countries was clear.

All of this changed with the rise of pluralism. Many countries now consist of citizens with divergent and at times opposing religious, cultural, and moral viewpoints. This is particularly true of the United States, whose citizens belong to a wide variety of religious and secular communities. Given such a diversity, the moral foundation of legislation and social policy is no longer clear. This helps explain why the many reports listed above make so little reference to the viewpoints of particular religious and secular traditions on the new treatments for infertility.

It is a mistake, however, to neglect these viewpoints. This is so for two reasons: (1) Even if pluralistic societies should formulate laws and social policies on neutral bases (whatever they may be), and without reference to the viewpoints of particular religious and secular traditions, individual members of these societies can be expected to continue to follow their own traditions. This will effect the extent to which such individual citizens accept and support the neutral policies. Social planners need to keep this in mind. Thus,in connection with the new reproductive technologies, members of particular traditions which oppose one or more of these techniques may not utilize them even if a neutral social policy permits utilization. Moreover, they may oppose public financing of their use, and may even advocate legislation against such use. Those planning public policies for the new reproductive technologies must therefore be aware of the diverse viewpoints of particular communities; (2) It is often unclear that there is a difference between a neutral social policy and a social policy based upon a secular tradition which emphasizes the appeal to individual autonomous choices described below. This reflection may lead some to desire to fashion a social policy for a pluralistic society which in some way synthesizes divergent traditions. Any attempt to do so will, of course, require careful attention to the beliefs of these viewpoints.

This report is an attempt to present the viewpoints of the many religious and secular communities in America on infertility prevention and treatment. It both surveys those viewpoints and attempts to predict their present and future impacts on individual choices and on community policy formulation.

PART II - SURVEY OF THE RELEVANT VIEWPOINTS OF AMERICA'S RELIGIOUS AND SECULAR COMMUNITIES

A. Overview of Issues

Before turning to a detailed examination of the views of particular religious and secular communities on infertility prevention and treatment, we need to have a basic overview of the relevant moral appeals which particular communities might or might not invoke as they examine these questions. This section of the report presents just such an overview.

1. Appeals to General Fundamental Moral Themes

One of the fundamental themes of much of modern moral thinking is the significance of free and autonomous choices. The exact definition of these concepts of freedom and autonomy is very controversial, but the basic idea seems to be that considerable moral significance is attached to a person's being free to make voluntary uncoerced choices based upon self-legislated principles and values. When this theme is applied to an evaluation of techniques for preventing and treating infertility, it leads to an emphasis on the moral significance of individuals and couples freely choosing to act in accordance with their own self-imposed values.

A second fundamental theme of much of modern moral thinking is the significance of considering the consequences of individual actions and/or social practices for all those affected by the individual actions and/or by the social practices. The individuals affected may be those who perform the actions and/or participate in the practices, or they may be other members of society who are affected. There is, to be sure, considerable controversy over how these consequences are to be identified and assessed, but the basic idea of this moral theme is relatively clear. When this theme is applied to an evaluation of techniques for preventing and treating infertility, it leads to an emphasis on evaluating the consequences of these techniques for the infertile couples, for their prospective children, and for the rest of society.

A third fundamental theme of much of modern moral thinking is the significance of recognizing the existence of deontological constraints on actions. The basic idea is that there are types of actions whose performance is morally illicit however valuable the consequences of the actions and however much the people involved want to perform them. Moral prohibitions (rules prohibiting these types of actions) express these constraints on actions. The exact nature of these constraints and the conditions under which they may be overridden are matters of great controversy, but the basic idea that there are such constraints which impose limitations on choices is relatively straightforward. When this theme is applied to an evaluation of techniques for preventing and treating infertility, it leads to an emphasis on examining whether particular techniques do or do not violate any of these constraints.

Most of the remaining moral appeals which we will now describe can, with some work, be subsumed under these three general fundamental moral themes. Nevertheless, it is of some value to describe them separately, since those who appeal to them often do so without subsuming them under some more general and fundamental moral theme.

2. Appeals to the Significance of Parenthood

Many religious and secular communities emphasize the moral significance of parenthood. There are several variations on this theme. One variation emphasizes the ways in which parenthood enriches the life of individual couples. A second variation emphasizes the importance of parenthood for the social order. These two variations are best viewed as instances of the appeal to consequences. Still a third variation emphasizes a theological dimension to parenthood. Parenthood is viewed as fulfilling a divine commitment to procreate, or is viewed as a way of human participation in the divine activity of creating and sustaining life. This third variation is best viewed as a special moral appeal, not reducible to any of the above-mentioned general and fundamental moral themes.

Any one of these variations on the theme of the moral significance of parenthood may have considerable relevance to a moral assessment of techniques for preventing and treating infertility. Depending upon a number of factors (e.g., the way in which a particular variation understands parenthood and the particular technique employed), this theme may lead to a very positive moral evaluation of techniques for preventing and treating infertility, techniques which may enable otherwise infertile couples to participate in parenthood.

Other religious and secular communities ascribe far less significance to parenthood. In some cases, parenthood is viewed simply as an option, one of no general moral significance, which individual couples can choose or not choose depending upon their personal goals and life-styles. In other communities, parenthood is conceived of as something which may actually interfere with morally more significant tasks of individual development. None of these communities will use an assessment of parenthood as a basis for positively evaluating techniques for preventing and treating infertility.

3. Appeals to Connections or Separations between Conjugal Sexuality and Reproduction

Most children who are born are the products of conjugal sexual relations. Many (if not most) acts of conjugal sexuality without contraception have at least the potential for resulting in conception leading to reproduction. These facts are understood very differently in different religious and secular communities.

Some religious and secular communities view these facts as having no particular moral significance. For these communities, these facts reflect nothing more than truths about the world before human beings intervene to change things. The development of contraceptive techniques enables couples to engage in acts of conjugal sexuality which no longer have reproductive potential. The development of some techniques for treating infertility enables couples to reproduce independently of acts of conjugal sexuality. None of this is morally objectionable to these communities, because they ascribe no moral significance to the pre-intervention connection between reproduction and conjugal sexual relations.

Other religious and secular communities see these facts very differently. For them, the pre-intervention connection between reproduction and conjugal sexuality reflects a natural order which should be respected. This leads these communities to conclude that contraceptive techniques which break the connection between conjugal sexuality and reproductive potential and techniques for treating infertility which break the connection between reproduction and conjugal sexuality are morally illicit. This is an appeal to a special type of deontological constraint on morally licit actions, the constraint of conformity to the natural order.

4. Appeals Relevant to only some Reproductive Technologies

The moral appeals which we have considered until now relate to the assessment of most if not all of the techniques for preventing and treating infertility. There are, in addition, special moral appeals which relate to one or more technique. These are appeals to specific deontological constraints, for they are arguments that particular techniques of prevention and/or treatment are illicit because they violate some moral rule. A partial list of such appeals includes the following: (a) Some communities believe in a moral prohibition against masturbation, whatever the intentions and purposes of particular acts of masturbation. Since infertility workups and forms of treatment often involve collecting sperm samples by masturbation, this moral constraint leads those communities to challenge the moral licitness of such workups and treatments; (b) Some communities accept a moral prohibition against adultery understood to cover not merely sexual acts but also reproductive acts where both of the gametes are not from a couple married to each other. Since some forms of treatment for infertility involve reproduction by use of gametes from persons not married to each other, such communities will reject those techniques on the grounds that they involve adultery. Other communities which are unwilling to see such acts as adulterous may still view them as morally illicit; (c) Some communities accept a moral prohibition against harming and destroying zygotes from the moment of conception. Since some forms of treatment for infertility involve producing multiple zygotes and destroying some of them, such communities will reject these techniques as morally illicit early abortions.

B. - The Viewpoints of the Various Religious Communities

1. The Roman Catholic Viewpoint

The Roman Catholic Church views itself as a direct continuation of the apostolic church founded by the authority of Jesus, and it views its head (the Pope, who is Bishop of Rome) as holding as position of authority analogous to that of Peter among the original Apostles. It perceives members of other Christian churches, such as the Eastern Orthodox churches and the Protestant churches, as Christians who have separated themselves from the true church. The Catholic church is episcopal in structure, with each of its dioceses presided over by a bishop who is viewed as a direct successor of the Apostles. Superimposed upon this episcopal structure is a central administration, the Roman Curia, presided over by the Pope. In addition, the Catholic church possesses a series of religious orders whose members (monks or nuns) devote themselves to special works and who are responsible to the officers of their orders which usually have their headquarters in Rome. In the United States, there are 164 dioceses and archodioceses (48).

The main sources of information employed in this report about the teachings of this church on the prevention and treatment of infertility are: (a) a series of statements issued by Pope Pius XII between 1949 and 1956 (38); (b) a large number of theological writings published between 1956 and 1986 and summarized in R. McCormick's Notes on Moral Theology ((35) and (36)), in J. C. Wakefield's Artful Childmaking (69), and in J. C. Nienstedt's Human Life in a Test Tube (42); (c) B. Ashley and K. D. O'Rourke's Health Care Ethics (4), a standard text published by the Catholic Health Association of the United States; (d) the recent statement by a curial body, the Congregation for the Doctrine of the Faith, entitled Instruction on Respect for Human Life in its Origin and on the Dignity of Procreation (12). Special attention will be paid to item (a) because of the special authority of the Pope and to item (d) because it is a crucial statement approved by the current Pope.

Pius XII spoke about the treatment of infertility on three occasions, when he addressed the Fourth International Congress of Catholic Doctors (in 1949), when he addressed the Italian midwives (in 1951), and when he addressed the Second World Congress on Fertility and Sterility (in 1956). In these three addresses, he made the following major points: (a) physicians must always consider new forms of treatment from the moral and judicial as well as from the biological and medical aspect; (b) procreation can only take place within matrimony and only when the gametes are from the husband and wife; (c) even artificial insemination using the husband's sperm is wrong, in part because it would be obtained by "acts against nature" (masturbation) and in part because it (like contraception) separates procreative activity from personal conjugal activities; (d) couples have no right to a child. The matrimonial contract only gives them the right to engage in conjugal acts which are destined to the end of childbirth; (e) for these reasons, in vitro fertilization must be rejected as immoral and absolutely illicit; (f) none of this forbids the use of artificial means designed to facilitate the sexual act or to enable it to attain its proper end of reproduction.

This set of papal teachings is the foundation of Ashley and O'Rourke's treatment of infertility problems in their standard text. Artificial insemination, using sperm from a donor or from the husband, is rejected, as is in vitro fertilization. Nevertheless, following Pius's suggestion, a number of techniques for helping reproduction through conjugal sexuality are allowed, including techniques for concentrating sperm density of semen emitted in intercourse, the use of a host surrogate mother providing that the zygote is a product of gametes from the husband and wife, and the removal of a mature ovum from the ovary to be returned to the fallopian tubes adjacent to the uterus in order to enable fertilization to take place in normal intercourse even when the fallopian tubes are blocked.

Ashley and O'Rourke were well aware that many Catholic theologians since the time of Pius XII were not in full agreement with his teachings. The main item of disagreement was the licitness of artificial insemination and/or in vitro fertilization using gametes from a husband and a wife. These dissenters argued that the unity of procreative activities and personal conjugal activities need not be present in every case of procreation or in every case of conjugal activity. Typical of the dissenting approach is the in vitro fertilization program at the Lille (France) medical faculty. The service is provided only to stable couples, they must provide the gametes themselves, all fertilized zygotes must be reimplanted in the prospective mother, and genetic experiments are prohibited.

This dissent within the Catholic Church was presumably one of the reasons why the Congregation for the Doctrine of the Faith issued its recent statement. That statement was based upon two principles, one arguing for respect for the human being from the moment of conception and the other arguing that procreation must take place in conjugal acts within marriage. In light of these basic principles, the teachings of Pius XII were reaffirmed with the following additions: (a) in vitro fertilization is now rejected for another reason, viz., the fact that many of the zygotes produced are often destroyed, thereby violating the principle of respect of life from conception; (b) freezing of embryos constitutes an offense against the respect due to human beings; (c) host surrogate motherhood is rejected even when the gametes come from a married couple and even when they are united through normal conjugal relations because it offends the dignity and rights of the child. It is clear then that official Roman Catholic teaching downplays the significance of parenthood to some extent, insists upon the connection between conjugal sexuality and reproductive potentiality, and embodies many deontological constraints.

Initial reactions to this latest document suggests that it is unlikely to end all dissent within the Catholic Church. Nevertheless, the following seems to be a summary of official Roman Catholic teachings, teachings which seem very firm at this point:

TABLE II B.1

(1) Interventions designed to augment the possibility of procreation through normal conjugal relations are morally licit.

(2) Infertility workups which involve masturbation are morally dubious.

(3) All forms of artificial insemination, in vitro fertilization, and surrogate motherhood are rejected as morally illicit for the reasons indicated above.

(4) The desire to procreate does not justify what is otherwise morally illicit.

2. The Eastern Orthodox Viewpoint

The Eastern Orthodox churches view themselves as a direct continuation of the undivided christian church of the first eight centuries which accepted the doctrinal decrees of the Seven Ecumenical Councils. This undivided church was split into two because of a schism between eastern and western christianity which began in the ninth century and was sealed by the sacking of Constantinople in 1204 by the Fourth Crusade. The resulting eastern church is divided today largely on ethnic and socio-cultural traditions into four patriarchates (bishops with the honor of primacy), eleven autocephalous (self-governing) and four autonomous but partially dependent churches, and ecclesiastical provinces in western Europe and North and South America which depend upon one of the autocephalous churches. In the United States, there are many Eastern Orthodox communities associated with different patriarchates and/or autocephalous churches. Most but not all are associated with the Standing Conference of Orthodox Bishops in the Americas, founded in 1960. The largest is the Greek Orthodox Archdiocese of North and South America, headed from 1949 to 1958 by Archbishop Michael, and since his death by Archbishop Iakovos (48).

The main sources of information employed in this report about the teachings of these churches on the prevention and treatment of infertility are: (a) *Statements on Moral and Social Concerns*, a document based upon the encyclicals of Archbishop Iakovos (16); (b) the writings of Stanley Harakas (25), former dean and currently professor of christian ethics at Holy Cross Greek Orthodox School of Theology, which summarize Eastern Orthodox teachings on these topics.

Some Eastern Orthodox theologians seen sexuality as a basically evil passion and see sexual relations as legitimate only when their intended purpose is to fulfill their natural purpose of procreation. Most, however, see sexual relations as having the intrinsic value of uniting husband and wife into a bond of mutual love and commitment. This larger group would accept the use of contraceptive devices so long as they were not used to permanently avoid the birth of any children. This latter condition is imposed because the birth of children is viewed as something very significant, in part as an expression of a loving physical and spiritual union and in part as a sharing with God in the creative activity. This attitude towards child bearing should lead to a general positive appraisal of the prevention and treatment of infertility.

Certain deontological constraints are generally recognized by this community. They include the following: (1) the unity of a marriage is violated not only by a third party joining one of the spouses in sexual relations but also by an outside party contributing genetic material to the creation of a child. This leads the Eastern Orthodox community to reject artificial insemination unless the sperm comes from the husband and the egg from the wife. It does not object, however, to artificial insemination using gametes from a married couple, despite the obtaining of the sperm by masturbation, and may even encourage that technique for use by otherwise infertile couples in light of the importance of procreation; (2) acts of killing zygotes from the moment of conception are murders, as decreed by the sixth Ecumenical Council in 691, and can only be justified to save the life of the mother. Since in vitro fertilization usually involves fertilizing several eggs and discarding all but one, Eastern Orthodox communities reject its use. Even if only one egg is fertilized, the Orthodox Church does not encourage the use of in vitro fertilization because of its separation of procreation from conjugal sexuality. That opposition is not expressed very strongly, however, and it is not entirely consistent with the Orthodox view of the licitness of separating the two in the use of contraception, so this teaching may change; (3) the use of a host mother to carry the fetus to term, even if the gametes used to produce the zygote come from a married couple, is said to be contrary to the Orthodox Christian ethic which emphasizes the spiritual and emotional relation to be formed between mother and baby during pregnancy. Again, this opposition is not expressed very strongly, is not entirely consistent with their support of adoption and their emphasis on the value of procreation, and may be open to change.

The following is a summary of Eastern Orthodox teachings:

TABLE II B.2

(1) Infertility workups and medical and surgical treatments of fertility for married couples are advisable because of the significance of procreation.

(2) A.I.H is also morally acceptable and may even be advisable if needed.

(3) A.I.D. is rejected as a form of adultery.

(4) In vitro fertilization is absolutely rejected when it invokes the destruction of zygotes and is not recommended even if only one egg is fertilized. That latter teaching has some potential for change.

(5) Host motherhood is rejected, whether or not the ovum cames from the wife. That teaching applied to the case when both gametes come from a married couple has some potential for change.

3. Interdenominational Protestant Viewpoints

The Protestant churches are a set of churches that trace their origin back to the Reformation in the sixteenth century. There are many different Protestant churches, divided into a number of major traditions, and we will be examining their individual viewpoints in the following sections. In this section, we will be examining a number of interdenominational Protestant viewpoints.

The main sources of information employed in this report about interdenominational Protestant viewpoints fall into two categories: (a) The writings of two major Protestant theologians (Joseph Fletcher and Paul Ramsey) who helped start the debate in Protestant circles about the treatment of infertility, and whose ideas have influenced, directly or indirectly, so much Protestant thinking since then; (b) several major statements by interdenominational groups, including the National Council of the Churches of Christ in the U.S.A.(39), the Working Party of the Free Church Federal Council and the British Council of Churches (21), and the World Council of Churches' Conference on Faith, Science, and the Future (72).

It is hard to imagine two theologians as radically different as Joseph Fletcher and Paul Ramsey. Fletcher's basic moral view is that love is the only standard of Christian morality. He understands that to mean that Christian moralists must judge each situation on its own (and not by reference to prescriptive laws), and that the situational judgment should approve the course of action that leads to the best ends or consequences. Not surprisingly, then, when Fletcher turns to the question of artificial insemination in his Morals and Medicine (20), he rejects what he takes to be the legalism of Catholic theology (their deontological constraints) on that topic. His approach leads him to accept the moral licitness of artificial insemination, whether the sperm comes from the husband or from another donor, because it may be the only means by which a couple's desire for a child may be satisfied. It would, presumably, lead him to accept in vitro fertilization. There are a number of psychological, social, and legal consequences of A.I.D. that trouble Fletcher, so he concludes that its practice would be inexpedient unless those problems could be resolved. Ramsey's basic moral stance on these issues (56) is radically different. He emphasizes the Christian insistence on the union between the unitive and procreative aspects of conjugal sexuality and on procreation growing out of a loving covenant between husband and wife, as a reflection of God's creation of the world because of His love. This leads him to reject such forms of infertility treatment as A.I.D., in vitro fertilization, host motherhood, etc. Unlike official Roman Catholic teaching, Ramsey accepts contraception which separates the unitive and procreative aspects in particular acts of conjugal sexuality but not in the whole series of acts of conjugal intercourse.

Given these fundamental disagreements among Protestant theologians, and given the disagreements to be documented below between different denominations, it is not surprising that interdenominational Protestant statements often avoid taking a stance on particular difficult questions in this area. Most typical of this approach is the statement from the National Council of the Churches of Christ which says that some (e.g., Roman Catholics, Ramsey) reject assisted reproduction because it separates procreation from conjugal sexuality while others (e.g., followers of Fletcher) accept it as a way of aiding infertile couples, while expressing concerns about such questions as the treatment of embryos. No position is taken in the statement about which side on this debate is correct. A very similar presentation is found in The World Council of Churches report, except for a definitive acceptance of A.I.H. Somewhat more definitive stands are adopted in the report of the working group from Britain. This is in large measure due to their moving beyond the traditional debate to emphasize certain themes of Protestant theology. The first is that children are fundamental to the Christian family, even though individuals might autonomously choose a vocation of childlessness for good reasons, so couples facing infertility problems should be aided in overcoming those problems. The second is that there are limits to what techniques may be employed, limits grounded in possible harmful consequences of infertility treatments, in possible infringements on the rights of others, and in the possibility of dehumanizing those who employ these techniques. All of this leads the working group to the following conclusions: (1) A.I.H. and in vitro fertilization using gametes from a married couple are morally licit, although the latter demands a thought out approach to the question of the unused zygotes and probably should not have a high priority for social funding in light of its expense and in light of other unmet health care needs; (2) All techniques for treating infertility should be employed only in connection with a married couple and must be based upon the consent of both spouses; (3) The group is badly split on the question of A.I.D. and in vitro fertilization using donor sperm. Some see these techniques as violative of the convenant of marriage just as adultery, while others see them as acceptable because of the consent of both spouses. Both groups are concerned, however, about a wide variety of consequences of their use (including issues raised by Fletcher), and all favor considerable hesitation in their use; (4) Surrogate and host motherhood are rejected because they dehumanize motherhood to nothing more than a biological process.

It is not easy to summarize such a wide variety of viewpoints, but the following table suggests the basic direction of current interdenominational Protestant thinking about the prevention and treatment of infertility:

TABLE II B.3

(1) The significance of procreation in the life of the community and in the life of individuals who want children leads to the appropriateness of society supporting the treatment of infertility for married couples so long as the treatment does not lead to a dehumanization of procreation and/or to a violation of convenental relations.

(2) The most acceptable treatments of infertility are the traditional medical and surgical interventions and A.I.H. In vito fertilization using gametes from a married couple and avoiding harm to any zygotes is probably also acceptable.

(3) A.I.D., in vitro fertilization not meeting the above requirements, and all forms of host and surrogate motherhood are at best morally questionable and at worst morally illicit.

4. Viewpoint of the Anglican Tradition

The Anglican tradition is a Protestant tradition which began in 1534 when an act of Parliament renounced the supremacy of the Pope over the Church in England, thereby establishing a national church headed by the King of England. Out of that national church grew a worldwide fellowship of independent churches sharing a common heritage, including the Book of Common Prayer, the doctrinal statements known as the Thirty-nine Articles, and an episcopal structure. There are 414 Anglican dioceses, located on every continent. The bishops of these dioceses meet every ten years in the Lambeth Conference held at the residence of the Archbishop of Canterbury, but that meeting has no legislative authority. The American branch of the Anglican tradition, called the Episcopal church, was founded in 1789. Its policy-making body is the General Convention which meets triennially, is composed of a house of bishops and a house of clerical and lay deputies, and has legislative power over the church in the United States (48).

The main sources of information employed in this report about the viewpoints of the Episcopalian Church on the presention and treatment of infertility are: (a) a series of relevant policy statements (24) adopted at the General Conventions of 1982 and 1985; (b) a report in 1977 of the Task Force on Human Life of the Anglican Church of Canada (15); (c) a summary of other Anglican ideas on this topic by David Smith (63) and by John Booty (6).

The crucial relevant policy decision of the 1982 General Convention was the decision approving in vitro fertilization using the husband's sperm when the cause of infertility is a physical defect in the reproductive tract of the wife. That decision was an extension of the 1973 decision which condoned the use of artificial insemination using the husband's sperm. It did not, however, go as far as the recommendation of the Standing Commission on Human Affairs and Health which approved of the use of male surrogates (in A.I.D.) but not the use of female surrogates because of the psychological risk to the surrogate mother and because of the possibility of her exploitation. The question of the disposition of the extra zygotes in vitro fertilization did not trouble the General Convention, presumably because it had approved abortion for significant reasons. Similarly, the question of the separation of procreation from conjugal sexuality did not trouble the General Convention, presumably because it had approved of contraception.

It is clear that the central issue currently debated in the Episcopalian Church in particular, and the Anglican community in general, is the licitness of a biological role for others besides the married couple in procreation. The Anglican tradition's concern with this issue goes back at least until 1948, when a commission appointed by the Archbishop of Canterbury challenged the moral licitness of A.I.D., arguing that it was a form of adultery, that it depersonalized sex by separating procreation from human relationships, and that it cast into doubt the physical kinship upon which the family is based. That issue was restudied by the Canadian Anglicans in 1977. The majority of the authors of their report argued for the licitness of A.I.D. when the husband is sterile on the grounds that children are a blessing which enrich marriage and society. A significant minority argued against its licitness on the basis of the deontological constraint that procreation should grow out of the personal intimacy of conjugal sexuality. All parties agreed, in opposition to the views of the Committee of 1948, that A.I.D. did not involve adultery. Smith, in the above mentioned book, sides with the minority and argues that surrogacy (either in the form of A.I.D. or surrogate motherhood) involves an act of hubris on the part of the fertile spouse. He argues that adoption, where both parents stand on an equal basis, is morally preferable.

The following is a summary of Anglican viewpoints on the prevention and treatment of infertility:

TABLE II B.4

(1) A.I.H. and in vitro fertilization using gametes from a married couple are morally licit. There seems to be no concern with the disposition of the unused zygotes in I.V.F.

(2) There is considerable controversy about the use of sperm from someone other than the husband in A.I.D. and in I.V.F., and that issue will continue to be controversial in the near future.

(3) There is general opposition to surrogate motherhood on grounds relating to the resulting depersonalization of motherhood and on grounds of potential exploitation. This opposition would apply whether or not the surrogate mother

donated the gamete or simply carried the implanted zygote to term.

5. Viewpoint of The Lutheran Tradition

The Lutheran tradition is a Protestant tradition which traces its roots to the teachings of Martin Luther, one of the founders of the Protestant Reformation. That tradition was particularly strong in northern Germany and in Scandinavia, and it was from those countries that immigrants brought Lutheranism to the United States. The churches which they brought to America were divided ethnically and linguistically, and the process of merging most of those churches into one united body is just now being completed. However, one component of the Lutheran tradition in the United States, the Lutheran Church-Missouri Synod, which is known for its uncompromising defense of Lutheran Orthodoxy, has remained independent of the merger movement. Both branches of the Lutheran movement have in recent years devoted more attention to matters of social policy, a reversal of the past where the great emphasis was on the mission and service work growing out of the pietist tradition in Lutheranism (48).

The main sources of information employed in this report about Lutheran viewpoints on the prevention and treatment of infertility are: (a) a 1981 report of the Commission on Theology and Church Relations of the Lutheran Church-Missouri Synod (10); (b) a series of essays ((30), (37), and (60)) on procreation ethics published by the Division for Mission in North America of the Lutheran Church in America; (c) a 1983 study of the Division of Theological Studies of the Lutheran Council in the U.S.A. (17), a group that brings together all branches of American Lutheranism.

The Lutheran Church-Missouri Synod report takes its point of departure from that denomination's understanding of marriage and sexuality. Marriage and conjugal sexuality have as their purposes the relational goal of mutual love, the procreational goal of having children, and the healing goal of restraining sin. All three of these goals must be joined together in the entirety of a relation, but not in each individual act of conjugal sexuality, so contraception within a union which is on the whole fruitful is morally licit. A.I.H. is viewed as morally licit because it promotes procreation within the general loving union of a husband and wife, even if the particular act of conception is not an act of conjugal sexuality. A.I.D. is rejected because it completely separates procreation from the loving union of husband and wife. The report does not extend this analysis to in vitro fertilization and surrogate motherhood, but promises to do so in a later study (not yet published) on biomedical ethics in general. But it has been extended to just these issues in the series of essays published by the Lutheran Church in America. In that analysis, I.V.F. is justified only when the gametes are supplied by a couple and only when all zygotes are implanted in the womb. Surrogate motherhood is also viewed as falling short of the Christian vision of procreation.

A somewhat more permissive attitude emerges in the 1983 study of the Lutheran Council in the U.S.A. The entire study group approves of I.V.F. when the gametes come from the married couple and when all the resulting zygotes are implanted in the wife's womb. But some members, for reasons that are not entirely clear, seem prepared to allow donor gametes and/or donor wombs. So there seems to be a shift developing in some portions of Lutheran thought.

The following table summarizes Lutheran viewpoints on the prevention and treatment of infertility:

TABLE II B.5

(1) Procreation within marriage is viewed as a positive blessing as well as a divine commandment, so the treatment of infertility is strongly encouraged.

(2) Procreative actions which take place within the general setting of a loving marital relation, even though the actual act of conception is divorced from it, are morally licit. Therefore, there is no objection to A.I.H. or to in vitro fertilization when it uses gametes and a womb from the married couple, and when all zygotes are implanted in that womb.

(3) A.I.D., in vitro fertilization not meeting the above conditions, and surrogate motherhood are generally opposed. That teaching may be open to change, however, in light of recent rethinkings of the issues by some in the Lutheran tradition.

6. Viewpoint of the Reformed Tradition

The Reformed churches are a series of Protestant churches which trace their origins to John Calvin, one of the major figures of the Protestant Reformation. Beginning in Switzerland, this branch of the Protestant movement spread into parts of France and Germany, into Holland, and into Scotland. The Heidelberg Catechism of 1563 and The Westminster Confession and Catechisms of 1648 were particularly important in defining Reformed beliefs in Europe and later in the United States, even though some of the most distinctive elements of those documents (e.g., predestination) were repudiated in the Reformed tradition during the first part of this century. The Reformed tradition split between those who placed primary authority in individual congregations (Congregationalists) and those who placed primary authority in elected central bodies, the presbyteries and the General Assembly (Presbyterians). The Pilgrims and the Puritans brought the former approach to America, while Scotch immigrants were central in bringing the latter approach to America. Today, all strands of the Reformed tradition are loosely united in the World Alliance of Reformed Churches (Presbyterian and Congregational). In the United States, the two largest Reformed communities are the Presbyterian Church and the United Church of Christ (which is a combination of the Congregationalists and the Evangelical and Reformed Churches) (48).

The main sources of information employed in this report about Reformed viewpoints on the prevention and treatment of infertility are: (1) two major documents adopted by the 1983 General Assembly of the Presbyterian Church, The Covenant of Life and the Caring Community (46) and Covenant and Creation: Theological Reflections on Contraception and Abortion (45); (2) Human Medicine, a book written by J. B. Nelson and J. A. S. Rohricht, a member of the United Church of Christ Advisory Board on Health and Human Services (41).

The Presbyterian documents present an approach to parenthood which stresses, on the one hand, the personal and religious significance of parenthood and, on the other hand, the need to covenant with one's children that parenthood will be responsible parenthood. These two attitudes lead Presbyterians to approve both of contraception and of medical and surgical techniques to alleviate the problem of infertility. Presbyterians are not in any way troubled by the separation of particular acts of conjugal sexuality from particular acts of procreation. They therefore also affirm the moral licitness of artificial insemination with sperm from the husband

and in vitro fertilization using gametes from a married couple. The relevant documents do not directly discuss the question of what to do with the unimplanted zygotes, although they do discourage their use in experimentation unless it is clearly of importance and no alternatives are available; the general pro-choice approach to abortion in Covenant and Creation suggests that a failure to implant some zygotes would be acceptable to Presbyterians. Finally, the 1983 documents, without much discussion, defer any decisions about A.I.D., I.V.F. using donor gametes, and surrogate motherhood until the psychological, legal, and ethical issues have been clarified.

Some of those unresolved issues are dealt with by Nelson and Rohricht in their book. They reject the claim that the of donor gametes constitutes a form of adultery on the grounds that such a view focuses on physical issues rather than on the intentions and relations involved. Adultery is a violation of the personal convenant in marriages, and the use of donor gametes undertaken out of freely-given mutual consent and out of a desire for a child that carries genetic material from at least one of the parents is not in violation of that convenant. They also reject the claim that A.I.D. and I.V.F. inappropriately separate procreation from conjugal sexuality. Given once more that the decision to use these techniques grows out of the above-listed factors, the use of A.I.D. and I.V.F. does involve procreation growing out of the relation (even if not the physical act) of conjugal sexuality. So they approve of both techniques, although they believe that I.V.F. is an inappropriate priority for public funding. Finally, they challenge surrogate motherhood because of its excessive separation of the emotional and relational aspects of pregnancy from motherhood, and argue against the use of A.I.D. and I.V.F. by single women on the grounds that the marriage convenant affords the appropriate context in which childbearing should take place.

The following table summarizes Reformed viewpoints on the prevention and treatment of infertility:

TABLE II B.6

(1) Responsible intentional procreation within marriage is viewed as a religiously significant action, so medical and surgical interventions to treat infertility are generally encouraged, even though contraception to avoid unintended procreation is also encouraged.

(2) There are no significant moral objections to the use of A.I.H. and in vitro fertilization using gametes from a married couple (regardless of the fact that some zygotes are not implanted).

(3) The use of A.I.D. and I.V.F. using donor gametes is more controversial, but will probably be treated as morally acceptable in the context of an infertile married couple mutually and freely choosing its use.

(4) Surrogate motherhood will probably be treated as illicit, in part because of psychological and relational issues and in part because of a fear of abuses.

7. Viewpoint of the Methodist Tradition

Methodists trace their origins to the late 1720s at Oxford University when John Wesley and like-minded students organized a group designed to recapture the piety and power of the early church. Their emphasis was upon fervor both in traditional religious activities and in good works. While originally a movement within the Anglican church, the Methodist churches clearly separated themselves to form a distinct religious community in the 1780s and 1790s. John Wesley visited the United States in the 1730s, and his new approach spread rapidly through the Americas. The American Methodist community split over racial and political conflicts in the nineteenth century, although many of these groups came together to form the United Methodist Church in 1968. Methodism was and is highly organized. Each national Methodist body conducts general conferences with bishops and lay representatives from which stem the highest enactments. The adopted policies are carried out by a network of boards and agencies (48).

The Methodist churches have a long tradition of issuing denominational statements on important social issues. In 1972, the General Conference of the United Methodist Church adopted a statement of social principles, and it has revised it every four years through 1984. An examination of that document reveals little that is relevant to our issues, except for a discussion of abortion that accepts it as legitimate when the life or well-being of the mother is threatened and that calls for thoughtful and prayerful consideration in all other cases. Moreover, despite the extensive involvement of the Methodist Church in founding and supporting health care institutions, the Methodist Church in America seems to have developed no other institutional traditions of reflecting upon the licitness of specific medical interventions. It would be inappropriate, however, to exclude the Methodist church from this study, so we have examined the writings on these issues of specific authors in some way associated with the Methodist Church. The main sources of information employed in this report about Methodist viewpoints on the prevention and treatment of infertility are: (a) Harmon Smith's Ethics and the New Medicine (64) and

(b) William B. and Priscilla W. Neaves's "Moral Dimensions of In Vitro Fertilization" (40).

Smith's presentation argues on behalf of A.I.H. (and, presumably, I.V.F. using gametes from a donor couple) and against A.I.D. (and, presumably, surrogate motherhood and I.V.F. using gametes from a donor). A.I.H., even if it involves masturbation and a separation of procreation from a particular act of conjugal sexuality, is still morally appropriate because the child is a product of a biological and personal union of the husband and wife. A.I.D., while it is not adultery in any sense, is still wrong because procreation is not a product of a mutual union. Smith adds the observation that there is no right to procreate, and that adoption remains an important option for couples. This analysis is reinforced in the Neaves essay, whose main goal is to butress the defense of I.V.F. using gametes from a married couple. They add the further requirements that I.V.F. should not be used for sex selection. They also approve of the practice of not fertilizing more ova than can be implanted. Finally, they offer a consequentialist argument for I.V.F. in light of the benefits it provides to infertile couples.

The following table summarizes Methodist discussions at this point on the prevention and treatment of infertility. It needs to be kept in mind that none of this is based upon official Methodist statements and/or publications:

TABLE II B.7

(1) Methodists insist upon the connection between procreation and conjugal sexuality only in that procreation is supposed to grow out of the physical and emotional union of a married couple.

(2) Therefore, they approve of A.I.H. and I.V.F. using gametes from a married couple, especially when all zygotes are implanted.

(3) They are concerned that I.V.F. not be used for sex selection or for the creation of experimental subjects.

(4) They are opposed to A.I.D., I.V.F. using donor gametes, and surrogate motherhood.

8. Viewpoint of the Mennonite Tradition

The Mennonite church derives from the Anabaptist movement in Switzerland, Germany, and the Netherlands in the sixteenth century, deriving its name from Menno Simons, one of the leaders of that movement. The Amish and the Hutterites are also descendants from the Anabaptists. Originally committed to the importance of adult rebaptism, the Mennonites came to add as distinctive doctrines a tradition of nonviolence, of a congregationally based church (although district conferences are now also important), of a total separation from the state, and of the use of church discipline to maintain standards of faith and life. The Mennonites came to America in a series of immigrations, including an eighteenth century Swiss migration to Pennsylvania and several nineteenth century Swiss, German, and Dutch migrations to the midwest and the prairie states (48).

In recent years, Mennonites have devoted much more attention than they have in the past to articulating an approach to sexuality and to related bioethical issues. This attention has resulted in two documents which are the main sources of information employed in this report about Mennonite viewpoints on the prevention and treatment of infertility: (a) a 1986 Resolution on Sexuality adopted by the General Conference Mennonite Church

(23) and (b) a working document of that community and of the Mennonite Church entitled Human Sexuality in the Christian Life (43).

Mennonites affirm the positive value of human sexuality independently of any procreative results, even while insisting that the satisfaction of these drives is not the chief good in life. Because the true gift of sexuality is its promotion of intimacy, premarital and extramarital sex are treated as immoral, but masturbation, as long as it is not used as a way of avoiding interpersonal relations, is acceptable. In light of all of these basic concepts, Mennonites accept contraception and the treatment of infertility by traditional medical and surgical interventions and by A.I.H., although these techniques are not stressed because the having of children is not a spiritual requirement. A.I.D. raises more serious issues, the most important of which is the introduction of a stranger into the procreative act. For Mennonites, the crucial question is whether adoping this technique strengthens or endangers the marital relationship and marital intimacy. A.I.D. and other forms of surrogacy would presumably be acceptable if that relationship and that intimacy is in fact enhanced.

The following table seems then to summarize Mennonite teaching on the prevention and treatment of infertility:

TABLE II B.8

(1) Both the single life and married life without children are religiously acceptable lifestyles, so there is no compelling religious need for infertile couples to pursue treatment of infertility.

(2) Such treatments are appropriate, however, if they strengthen the marital relationship and marital intimacy.

(3) Since there need be no connection between particular acts of conjugal sexuality and reproduction, A.I.H. and I.V.F. are acceptable.

(4) A.I.D. and (presumably) host motherhood are acceptable, so long as they strengthen the marital relation and marital intimacy.

9. Viewpoint of the Baptist Tradition

Baptists trace their roots to English puritanism with its emphasis on baptism of convinced believers, on a congregational structure without a clerical hierarchy, and on an avoidance of binding creeds so that individuals might derive new truths from their own study of the Bible. The first Baptist church was established in England in 1612, and Roger Williams formed the first Baptist Church in America in 1639. The great periods of growth of the Baptist church were, however, during the First Great Awakening in the 1740s and during the Second Great Awakening in the beginning of the nineteenth century. Baptists then began to join together to promote missions and to promote religious education and publishing, but they retained a fierce commitment to congregational independence, and their history has been marked by division and controversy. The largest Baptist groups in America are the Southern Baptist Convention, two Black Baptist Groups (the National Baptist Convention of the U.S.A. and the National Baptist Convention of America), and several northern Baptist Groups (48).

Baptists have neither a tradition of statements by their conventions on biomedical issues nor an extensive theological literature devoted to issues of bioethics. The abortion issue has been an exception to this. While the 1971 Southern Baptist Convention voted to support abortion in cases of rape, incest, and fetal deformity, as well as in cases of threats to the health and/or life of the mother, Southern Baptist opinion has changed rapidly. Since 1980, Southern Baptists have supported a constitutional amendment to prohibit abortions except to save the life of the mother (71). As part of this changed interest, the Christian Life Commission of the Southern Baptist Convention published in 1981 a pamphlet *Issues and Answers: Biomedical Ethics* (9), which raises many of our questions, although it does not offer any answers to them. As a result, at least one prominent Southern Baptist theologian, Paul D. Simmons, has written an analysis of many bioethical issues in his *Birth and Death: Bioethical Decision-Making* (61), and it will be used as the main source of information employed in this report about Baptist viewpoints on the prevention and treatment of infertility. It is used, however, with some caution, because Simmons's attitude towards abortion is certainly more permissive than the attitude which has become the majority viewpoint in the Southern Baptist Convention, and this may also be true about his attitude towards other questions.

Simmons, like all other Southern Baptist theologians, attempts to base his discussion on a Biblical approach. What he is seeking, however, is neither rules nor casuistic details but rather Biblical perspectives. His first perspective is that marital sexuality has significance independently of any procreative intent. This leads him to reaffirm the traditional Southern Baptist attitude towards the permissibility of contraception. A second perspective is that infertility is seen in the Bible both as a personal frustration and as a theological issue in that God wants people to experience the gift and power of procreation. This perspective, reinforced by an appeal to various stories about the patriarchs, leads him to the conclusion that infertility should not be viewed as the will of God to be passively accepted, but as a challenge to be surmounted so that God's blessing of procreation can be realized. If handmaids (Hagar, Bilhah, and Zilpah) were acceptable as a way of dealing with infertility, he argues, surely artificial interventions should be acceptable as well. A third perspective is that it is the intention to bring forth a child out of a loving stable relation that is a necessary condition for the legitimacy of any procreative act. A final perception (one which is not representative of general Southern Baptist teaching) is that fetuses only have anticipatory personhood. In light of all of these perspectives, Simmons concludes with a positive appraisal of the new reproductive technology. Of some interest is that he approves of them regardless of the source of the gametes, without considering all of the familiar questions about adultery, the marital bond, etc. It is likely that this is the area, if any, in which other Southern Baptists might disagree. Evidence for this will be provided below in our discussion of fundamentalist/evangelical viewpoints.

The following table summarizes Southern Baptist discussions at this point on the prevention and treatment of infertility. It needs to be kept in mind, however, that none of this is based upon official Southern Baptist statements and/or publications:

TABLE II B.9

(1) There is no necessary connection between individual procreative acts and individual acts of conjugal sexuality.

(2) Procreation is a blessing, and a biblical attitude approves of artificial attempts to make procreation possible. This justifies traditional infertility workups and treatments. It also justifies A.I.H., A.I.D., and I.V.F. Some Southern

Baptists may, however, oppose the use of techniques involving donor gametes.

(3) Since fetuses, especially at the earliest stages, only have anticipatory personhood, abortion concerns are irrelevant to the new reproductive technologies. However, in light of recent Southern Baptist statements about abortion, some Southern Baptists may prefer limiting I.V.F. to cases in which all zygotes are implanted.

10. Viewpoint of the Evangelical-Fundamentalist Tradition

Evangelicalism in its broadest sense represents that movement within Protestantism which emphasizes the need for personal conversion for salvation. Both the first and second awakenings in America led to the spread of evangelicalism in that broad sense in most Protestant denominations, especially the Methodist and the Baptist. This form of religious experience was challenged by the rise of modernist thinking in the second half of the nineteenth and the first part of the twentieth centuries. This led to a reaction which produced the modern Evangelical-Fundamentalist tradition. The first wave of this tradition produced, in the period 1910-1915, the twelve volumes called The Fundamentals and the formation of a series of separatist denominations, seminaries, and mission agencies. The second wave which started in the 1950s and continues until today, produced an extensive network of neo-evangelical non-denominational schools and seminaries, parachurch organizations, periodicals and publishing houses. While both waves agreed on a belief in the full inspiration and complete infallibility of the Bible, the recent neo-evangelicals have encouraged evangelical scholarship and a social consciousness which leads them to address bioethical questions (44) and (48).

The main sources of information employed in this report about Evangelical-Fundamentalist viewpoints on the prevention and treatment of infertility are: (a) N. L. Geisler's *Ethics: Alternatives and Issues* (22); (b) D. Gareth Jones's *Brave New People* (31); (c) a series of articles ((2) and (67)) in evangelical journals devoted to these issues. It is important to keep in mind, however, that this literature, like the literature we analyzed from the Methodist and Southern Baptist traditions, represents individual opinions in a tradition which downplays the significance of denominational statements.

Geisler's analysis begins with certain familiar Protestant viewpoints about sexuality and procreation. Sex has unificational and recreational purposes which are independent of procreative purposes, and procreation is only a general obligation on the species, one which individals may avoid entirely or at least limit. These points justify a separation of individual acts of procreation from individual acts of conjugal sexuality, thereby justifying A.I.H. To these familiar themes, Geisler adds the observation that the Old Testament commandment to raise up seed to one's deceased brother by inseminating his wife (*Deut.* 25:5) indicates that being childless and heirless is a burden to be avoided by extraordinary means. A.I.D., he concludes, is an improvement made possible by new technology, one which should be adopted. Moreover, there is no problem with adultery because the Biblical opposition to adultery is just an opposition to a sexual union of persons not properly married.

It is on this last point that Geisler's analysis is challenged by many others in the Evangelical-Fundamentalist tradition. Jones, for example, insists that A.I.D., I.V.F. using donor gametes, and surrogate motherhood are not acceptable. While agreeing that they are not adultery, since no breach of faith is involved, Jones opposes them because they separate the biological and personal aspects of parenthood and the love-making and life-giving facets of marriage. In addition, I.V.F. raises for Jones the issue of embryonic wastage, an important issue for evangelicals who have come out very strongly against abortion. Jones's approach seems to be supported by the Christian Medical Society and by most of the recent evangelical articles discussing these issues.

The following table summarizes evangelical-fundamentalist discussions at this point on the prevention and treatment of infertility. It needs to be kept in mind, however, that none of this is based upon official statements and/or publications:

TABLE II B.10

(1) While there is no absolute commandment on each individual couple to procreate, infertility is viewed in the Bible as a burden to overcome. This leads to a positive evaluation of infertility workups and treatments.

(2) In particular, because individual acts of conjugal sexuality and individual acts of procreation can be separated from each other, there are no moral objections to A.I.H. and I.V.F. using gametes from a married couple.

(3) There is considerable controversy over A.I.D., I.V.F. using donor gametes, and surrogate motherhood. Many oppose these techniques although they do not see them as adultery. Others find them as contemporary improvements over Biblical analogues. Recent evangelical treatments support the former position.

11. Viewpoint of the Seventh-Day Adventist Tradition

The Seventh-Day Adventists trace their ancestry back to the 1840s when William Miller predicted that Christ would return on October 22, 1844. After the failure of that prediction, Miller's movement split into several groups, the most important of which became the Seventh-Day Adventist Church, who believed that Ellen G. White had the spirit of prophecy. From the very beginning of her prophecies, Mrs. White sketched a gospel of health which included avoiding medications and seeking health through proper diet (no alcohol, tobacco, caffeinated beverages, and meat). While there have been considerable changes in the movement since her death, the Seventh-Day Adventists have continued their emphasis upon health by creating a large network of health-related institutions capped by the various schools at Loma Linda University. While Seventh-Day Adventists accept current medical therapeutics, their hospitals still discourage drinking, smoking, and meat eating, eschew optional treatments on the Sabbath, and emphasize a sense of the presence of God throughout the healing process (44).

Starting in the 1960s, the Seventh-Day Adventists began to address bioethical issues. They were led in this process by Jack Provonsha, a physician on the faculty of Loma Linda University, and by Roy Branson, who taught ethics at a Seventh-Day Adventist Seminary in Michigan. This led to the formation of a Center for Christian Bioethics at Loma Linda University in the early 1980s. When we could not find any published Seventh-Day Adventist material, we turned to that center which sent us two unpublished lectures of Dr. Provonsha ((49) and (50)) and some data on A.I.D. and I.V.F. programs in Seventh-Day Adventist hospitals (33). This material is our source of information for this report about Seventh-Day Adventist viewpoints concerning the prevention and treatment of infertility.

Provonsha argues that the Biblical prohibitions and rules, on the one hand, and the Levirate practices and the stories of Hagar, on the other hand, do not, contrary to many Biblical-based authors described above, really settle the questions raised by the newer reproductive techniques. Seventh-Day Adventists need to turn, therefore, to the ways in which nature shows us that human life is unique. Provonsha identifies two such messages from nature. The first is that human reproduction should be a love act. The second is that reproduction carries with it a responsibility for the children involved. This leads him to object to using donor gametes, where there is no donor love act and where the donor has no responsibility for his genetic offspring. As a result, Provonsha challenges the licitness of A.I.D., I.V.F. using donor gametes, and surrogate motherhood. He finds the commercialization of the surrogacy arrangements an additional objection to those arrangements. However, Provonsha does approve of traditional infertility treatments, A.I.H., and I.V.F. using gametes from a married couple, as they meet the conditions that reproduction grows out of a love act and entails a responsibility for the children involved.

The staff of the Center for Christian Bioethics at Loma Linda University inform us that Loma Linda and other Seventh-Day Adventist institutions utilize A.I.D. and donor gametes in their new I.V.F. program. So Seventh-Day Adventist opinion is clearly split on these topics. The least support, we are told, is found for commercial surrogacy.

The following table summarizes the current state of Seventh-Day Adventist thinking on the prevention and treatment of infertility. It is important to keep in mind, however, that none of this is based upon official statements and/or publications:

TABLE II B.11

(1) Given the legitimacy of separating individual acts of conjugal sexuality from individual acts of procreation, there are no moral objections to traditional workups and treatments of infertility and to A.I.H. or I.V.F. using gametes from a married couple.

(2) A.I.D. and I.V.F. using donor gametes are more controversial, with some Seventh-Day Adventists opposing them while Seventh-Day Adventist institutions are using them.

(3) There is little support for commericalized surrogacy.

12. Viewpoint of the Christian Science Church

The Christian Science Church grew out of Mary Baker Eddy's spontaneous recovery from a severe injury in 1866, a recovery that authenticated for her the belief that evil and disease are only illusions which can be healed by a patient's coming to recognize the metaphysical truth about her illness. These new teachings were summarized in her Science and Health, whose first edition appeared in 1875. After considerable turmoil, the resulting church was reorganized by Eddy. She established a central church organization, the Mother Church in Boston, a board of directors to oversee its affairs, and a publishing society whose most famous publication is a newspaper, The Christian Science Monitor. After her death, a conflict arose between the Board of Directors and the Trustees of the Publication Society. It was resolved in 1922 when the Board of Directors was given full control of the Church. There is no ordained clergy in the Christian

Science Church so, despite the strong organizational control, moral decisions are left to the prayerful consideration of individual members (44).

We can identify no immediately relevant Christian Science literature. There have been a number of editorials and columns in the Christian Science Monitor about reproductive issues, but they raise few of the considerations which are distinctive of Christian Science thought. We shall attempt to project, therefore, a Christian Science viewpoint based upon an understanding of their general world view. We have been helped in this process by guidance from the Manager of the Committee on Publication of the Mother Church (66).

From the very beginning, Christian Scientists eschewed the use of drugs and surgical interventions to treat illnesses. Instead, Christian Scientists turned to practitioners who heal through the process of prayer and reflection described as demonstration. Coming to think the truth about the illusion of evil (demonstrating it) causes the apparent symptoms to vanish into nothingness (thereby demonstrating again the truth of the claim that evil is an illusion). Some exceptions were made by Mrs. Eddy for bonesetting and for the use of obstetricians during child birth. All of this suggests that Christian Scientists would see various aspects of reproductive technology as inappropriate responses to infertility rather than as morally questionable acts. This opposition would be particularly significant for more traditional techniques which involve drugs and/or surgery and for in vitro fertilization which does as well. It would be less significant for artificial insemination which does not. But turning to God for the healing of infertility might be the most appropriate Christian Science response, even if individuals choose to use techniques, such as artificial insemination, which involve neither surgery nor drugs.

The following chart summarizes the hypothesized Christian Science viewpoint on these issues:

TABLE II B.12

(1) The best treatment for infertility is prayer which dispels the illusions which are the source of the problem.

(2) Individuals may choose to supplement that with techniques (such as artificial insemination) which employ neither drugs nor surgery, but techniques which do (including in vitro fertilization) are inconsistent with the basic Christian Scientist viewpoint.

13. Viewpoint of the Jehovah's Witnesses

The Jehovah's Witnesses were founded in 1879 by Charles Taze Russell who headed that group until his death in 1916. The church he founded ultimately evolved into a highly centralized authoritarian organization headed by Joseph F. Rutherfold until his death in 1942 and by Nathan Knorr from 1942 to 1977. Since the mid-1970s leadership of the church has been in the hands of a collegium of eighteen members who make decisions by a 2/3 vote and whose decisions are widely disseminated through the publications of the Watchtower Bible and Tract Society and through a very active missionary program. Fundamental to this religion is the belief that the Battle of Armageddon will soon be fought, that only Witnesses will survive that conflict, and that 144,000 annointed will then rule with Christ while the billions who are resurrected are given a chance to prove themselves worthy of eternal life. Among the distinctive practices of the Jehovah's Witnesses are a refusal to participate in the political process (they do not vote, hold public office, or salute the flag) and a refusal to undergo blood transfusions. These practices have often led them into conflict with other segments of society (44).

The sources employed in this report for information about the viewpoint of Jehovah's Witnesses about the prevention and treatment of infertility are: (a) statements in The Watchtower on children and adoption (52), on IUDs and early abortions ((51) and (53)), on I.V.F. (54), and on surrogacy (27); (b) chapters 13 and 14 of True Peace and Security, a pamphlet published by the Watchtower Bible and Tract Society (70).

Jehovah's Witnesses do not ascribe the same significance to parenthood as do other religious traditions. They point out that childlessness often allows couples more time for the service of God. Having children is purely a matter of individual choice. Therefore, they have no strong reasons to encourage the treatment of infertility. Nevertheless, they would not object to such treatments providing that certain deontological constraints are observed. They include: (a) the gametes must come from the husband and wife and not from a third party (or from an unmarried couple), because this would violate the biblical prohibitions (in Leviticus) against adultery (or fornication) which are formulated in terms of the providing of semen to others; (b) there must be no possibility of an abortion of the zygote from the moment of conception, for that is the point at which human life is entitled to respect. As a result, Jehovah's Witnesses could approve of A.I.H. and I.V.F. if gametes from a married couple are employed and if no zygotes are destroyed. They would have to disapprove of A.I.D., of surrogate motherhood, and of I.V.F. unless the above-mentioned conditions are satisfied. They are also concerned that the nutrients involved in nourishing the zygotes in I.V.F. involve no blood products.

The following table summarizes the viewpoints of the Jehovah's Witnesses on the prevention and treatment of infertility:

(1) Infertility workups and traditional medical and surgical interventions are morally licit but are neither encouraged nor discouraged because no particular moral significance is ascribed to parenthood.

(2) A.I.H. is morally licit, as is I.V.F. providing that the gametes come from the married couple, providing that no zygotes are destroyed, and providing that no blood products are employed.

(3) A.I.D., surrogate motherhood, and I.V.F. (if the above conditions are not satisfied) are serious violations of some of God's fundamental laws.

14. Viewpoint of the Mormon Church

The Mormon Church (Church of Jesus Christ of Latter-Day Saints) was organized in 1830 in upstate New York by Joseph Smith. After several moves by the believers, and after Joseph Smith was killed in 1844, his successor, Brigham Young, led the church to what became its international headquarters in Utah. There, the church has grown to a significant presence in the religious life of the United States. Joseph Smith had already begun the conception of a church with a hierarchical style of leadership culminating in a president to whom new prophecies are sometimes granted. This form of leadership continues until today (44).

We have not been able to identify relevant Mormon literature specifically addressing the question of the new reproductive technologies. However, the Director of Public Communications of the Mormon Church in Salt Lake City was kind enough to provide us with a brief summary of how the church currently counsels its members on these topics (8). This synopsis confirms the analysis of Lester Bush in his article "Ethical Issues in Reproductive Medicine: A Mormon Perspective" (7).

Mormons have a very positive attitude towards procreation because it fulfills the Divine commandment to multiply and because it is a source of joy in one's posterity. This originally led church president Joseph F. Smith in 1908 to reject birth control except in cases of sickly individuals or those with genetic problems. Over the years, this teaching has been further modified to allow for proper spacing of children and to take into account the family's economic capacities. Still, the Mormon ideal is that of a larger family than is currently common in America. All of this should lead to an approval of techniques for aiding fertility. Still, certain deontological constraints are present. A strong opposition both to adultery and to fornication has carried over to a negative evaluation of A.I.D. and of artificial insemination of single women; however, the former is not viewed as adultery, and is now described as discouraged but an option to be decided upon by the husband and wife upon whom the decisional responsibility rests. In vitro fertilization is not viewed as raising any intrinsic moral problems, but the concern about the use of donor sperm remains. No mention is made of the issue of unused zygotes, but given the Mormon emphatic opposition to abortion (described as one of the most revolting and sinful practices), one can hypothesize that Mormons would insist upon the implantation of all zygotes. Finally, in addition to any of the above issues, surrogate motherhood is discouraged because of possible psychological problems for the surrogate and/or for the couple.

The following table best summarizes what can be surmised about the viewpoints of the Mormon Church on the prevention and treatment of infertility:

TABLE II B.18

(1) Because of their great emphasis on procreation, Mormons would encourage infertility workups, the traditional medical and surgical interventions, and artificial insemination and in vitro fertilization using gametes from the married couple.

(2) A.I.D. is not encouraged, but is left as an option for couples. Surrogate motherhood is definitely discouraged. Because of the lack of a definite prohibition, this is a viewpoint that has potential for change.

(3) The disposal of non-implanted zygotes in I.V.F. may well be prohibited as a form of abortion.

15. Viewpoints of the Jewish Traditions - Orthodox, Conservative, and Reform

Judaism was the first of the monotheistic faiths of the west. It accepts only the Old Testament as God's bible, but it also accepts as authoritative the rabbinic law which grew out of the Old Testament, was codified in the Mishna and in the Talmud, and continues to be expounded until today by the rabbinic leadership of the Jewish community. One of the great issues in Judaism since the Englightenment is the relation between this traditional Jewish law and thought and the ideas and practices of the contemporary world. The Jewish community eventually split over this issue into three major groups. The Orthodox movement accepts the continued validity of biblical and rabbinic law and insists upon organizing life in the contemporary world so as to be compatible with that law. The Reform movement places far greater emphasis upon accepting the insights of modern thought and upon modifying Jewish life in accordance with these insights, while at the same time being faithful to what it takes to be the fundamental insights of Jewish tradition. In between these two extremes lies the Conservative movement, which is more faithful to the details of Jewish tradition than the Reform movement while more open to changes than the Orthodox movement. All three of these movements have significant representation among American Jews, a community which is primarily derived from European Jewish immigrants who came to America in the period 1840-1920.

The sources employed in this report for Jewish viewpoints on the prevention and treatment of infertility are: (a) *Compendium on Medical Ethics*, an interdenominational publication (19); (b) Orthodox rabbinic viewpoints summarized in J. David Bleich's *Judaism and Healing* (5) and Avraham Steinberg's *Jewish Medical Law* (65) and explained in practice in J. Schenker's *report* (59) on the I.V.F. program at Hadassah Hospital in Jerusalem; (c) Conservative viewpoints described in material obtained from the archives of the Committee on Jewish Law and Standards (34); (d) A series of Reform rabbinic opinions collected in Walter Jacobs's *American Reform Responsa* (28) and *Contemporary American Reform Responsa* (29).

The interdenominational *Compendium* exhibits the strains of attempting to compromise among several different traditions. It begins with a strong endorsement, in light of the commandment to procreate, of infertility workups and A.I.H., subject only to the condition that attempts be made, if possible, to obtain the sperm without acts of manual masturbation. A.I.D. and I.V.F. using donor sperm are treated very differently. The *Compendium* insists that neither involves adultery and that there is no question of the illegitimacy of the resulting child. Nevertheless, both are discouraged, in part because they weaken the parent-child unit and in part because of the possibility of incest due to the secret paternity of the child. Having said that, the Compendium seems to allow both in the absence of an alternative. So its actual view is not well defined. It is much clearer on the question of extra zygotes in I.V.F. Such zygotes are viewed as not having human rights, and they can be discarded or used for research. In order to understand the conflicts behind the formula of the Compendium, we turn to an examination of the viewpoints of the three major denominations.

The Reform movement first considered questions of the new treatments of infertility in 1952. Its early leadership agreed that all efforts should be made to help infertile couples, in part to meet the individual's need to procreate and in part because of the Jewish community's need to meet the challenge of a declining population. All of its authorities in 1952 approved of A.I.H., but they were split over A.I.D., although all agreed that it did not involve any question of adultery. By the 1970s, Reform opinion had definitely accepted A.I.D., and it therefore was not troubled by that aspect of I.V.F. or of surrogate motherhood. Also, Reform opinion had concluded that fetuses below the age of 40 days were not in any way persons and could be used for experimentation, so there would be no problem with disposing of unimplanted zygotes in I.V.F. The Reform movement continues to have some hesitations about I.V.F. and surrogate motherhood, but they are consequentalist concerns about psychological and legal implications of the use of these techniques.

Orthodox opinion has been very different on these topics. A.I.H. is permitted as long as the husband's semen is obtained, if possible, without masturbation. A.I.D. is, however, rejected. Some authorities view it as adultery, and view the resulting children as illegitimate, even though no sexual intercourse is involved. Those who do not reject it on grounds of adultery still reject it, either because it violates the principle that paternal identity should not be concealed or because it gives rise to the possibility of future unintended incest. These same principles when applied to I.V.F. allow its use only when the gametes are from a married couple. The question of the extra zygotes has troubled Orthodox authorities. Some have no objection to feticide in the first 40 days, while others view abortion as illegitimate from the moment of conception. Therefore, Orthodox opinion prefers the fertilization of a single ovum. The Hadassah Hospital I.V.F. program follows all of these Orthodox restrictions.

Conservative Jewish opinion has evolved over a period of time. The Committee on Law and Standards in 1967 opposed A.I.D. for essentially the same reasons found in the Orthodox literature. Even then, however, leading Conservative figures were far from unanimous in that opposition. In more recent years, most Conservative authors have come to accept the legitimacy of A.I.D. with the consent of the husband as a final alternative when nothing else has helped. This seems to be emerging as the attitude towards I.V.F. as well. Finally, with similar reservations, the Law Committee approved in 1985 the practice of surrogate motherhood.

The following table summarizes the teachings of Judaism on the prevention and treatment of infertility:

TABLE II B.15

(1) Because of the religious and personal significance of procreation, traditional infertility workups and treatments

are encouraged, subject to the constraint of minimizing the use of masturbation.

(2) A.I.H. is acceptable, as is I.V.F., when it uses gametes from a married couple and when all zygotes are implanted.

(3) A.I.D., I.V.F. using gametes from a third party, and surrogate motherhood are more controversial. They are acceptable to Reform Judaism and are increasingly acceptable as a last alternative to Conservative Judaism, but are rejected by Orthodox Judaism.

16. Viewpoint of the Islamic Tradition

The Islamic tradition was founded by the Prophet Muhammad (570-632). Its fundamental beliefs include a belief in one God, Allah, and in his messenger, Muhammad. The definitive sources of Islamic doctrine and practice are the Quran and the Sunna, both connected with Muhammad. The Quran consists of messages which Muhammad received from Allah from 610 until 632. The Sunna consists of hadiths, reports of the precepts and deeds of Muhammad. There are six canonical collections of hadiths, dating to the ninth century, accepted by Sunni Muslims. The Shi'ite Muslims have their own collections of hadiths, but 90% of them relate to Shi'ite Imams and not to Muhammad. The Muslim religion spread over the centuries through North Africa, the Near East, and much of Asia (including Iran, Pakistan, and Indonesia). Immigrants from those predominantly Muslim countries brought Islam to the United States.

The sources employed in this report for Islamic viewpoints on the prevention and treatment of infertility are: (a) Dr. Yusuf Al-Qaradawi's Al-Halal Wal-Haram Fil-Islam (The Lawful and the Prohibited in Islam) (1), a detailed account of Islamic law as it applies to Muslims living in Europe and America in the twentieth century; (b) Fazlur Rahman's forthcoming Health and Medicine in the Islamic Tradition (55).

Islam ascribes great significance to the having of children. Besides any personal considerations, the having of children is given great religious significance. An important hadith reports Muhammad as saying that his followers should reproduce and increase in number and that this would lead him to be proud of the number of his followers on the Day of Resurrection. Therefore, Islam would welcome infertility workups and treatments. Moreover, it would have no problem either with the masturbation involved, or with the separation of reproduction from conjugal sexuality, since it has traditionally accepted the former when necessary and it has allowed the separation involved in the latter in cases of contraception. Nevertheless, there are important deontological constraints which would limit the acceptability of some of the new reproductive techniques. Besides recognizing the grave sin of adultery, Islam recognizes as a significant sin the confusion of lineage. For this reason, it prohibits full adoption, although it allows someone to rear an orphan as long as he makes it clear that the orphan is not his child. Even if A.I.D. is not viewed as adultery, it would certainly be viewed as a violation of this other prohibition. This prohibition has significant implications for cases of I.V.F. using donor sperm as well. Another important deontological constraint is the prohibition against abortion, with its implications for what may or may not be done with the extra zygotes often obtained in I.V.F. Some Muslim authorities allow abortion for the first four months after conception before the fetus is infused with life. Others see early abortions as wrong, although not as wrong as later abortions.

There is one additional aspect of this issue which should be mentioned. Islam allows for polygamy, subject to the condition that the husband can deal equitably with each wife and subject to the condition that the total number of wives should not exceed four. One of the reasons traditionally given for multiple wives was to allow a man to remain married to a first wife who was infertile while marrying a second wife to have children. This traditional approach offers Muslims an alternative approach to dealing with infertility in certain cases. Whether this alternative is acceptable to contemporary western Muslims is a question whose answer remains unclear.

The following table summarizes the teachings of Islam on the prevention and treatment of infertility:

TABLE II B.16

(1) Because of the great significance of reproduction, Islam would welcome effective infertility workups and treatments and would not be troubled by their use of masturbation.

(2) Muslims would have no problems with A.I.H. and with I.V.F. when both gametes come from a married couple and when all zygotes are implanted.

(3) A.I.D. and I.V.F. using donor sperm would be rejected on the grounds that they confuse lineage, and they might also be rejected as forms of adultery. A failure to implant all zygotes in I.V.F. might be prohibited (although not strongly) as a form of early abortion.

17. Viewpoints of Other Religious Traditions

This survey, as extensive as it has been, by no means covers all of America's religious traditions. In this section, we briefly indicate the major remaining traditions and the reasons for not covering them.

There are an increasing number of Asian-Americans whose religious viewpoints are rooted in such religions as Hinduism, Buddhism, and Confucianism. These are old and rich traditions, with extensive views on human sexuality, on reproduction, on nature and technology, etc. However, we could find no evidence that contemporary scholars in those traditions were attempting to apply those views to our issues. It seemed inappropriate to attempt to do so on our own.

America has a great many religious communities which grow out of the Afro-American experience. They range in size from major segments of the Methodist and Baptist traditions to santeria and voodoo centers. We were unable to find any material from these communities addressing our issues, so we cannot ascertain what these religious groups think about the new reproductive technologies. In particular, we cannot say whether general Methodist and Baptist viewpoints would be equally shared by the major black Methodist and Baptist churches.

We have also left out a number of major Protestant denominations. The Pentecostalist churches, particularly the Assemblies of God, have, we are told, specifically chosen not to address what they take to be social issues such as questions surrounding the new reproductive technologies. We could not find any material coming from such diverse groups as the Churches of Christ/Disciples of Christ, the Quakers, and the Unitarian-Universalist Church.

Finally, America's indigenous population, the Native Americans, have their own very rich traditions. For all of the above reasons, we were unable to report on their attitudes towards these questions.

Despite all of these gaps, we have presented a rich and diverse set of religious views concerning the prevention and treatment of infertility. We will now turn to a presentation of some secular viewpoints, and then to some summation of what we have discovered.

C. Various Secular Viewpoints

1. The Viewpoints of Scholars Writing Independently of an Organized Community

Discussions of bioethics are enriched by the contributions of many scholars drawn from a wide variety of disciplines (philosophy, law, medicine, economics) who analyze bioethical issues from a secular perspective. This general observation is particularly true of questions surrounding the prevention and treatment of infertility, so any account of the various viewpoints on these questions would be seriously incomplete if it failed to include some account of these authors.

It is impossible to summarize all of this secular literature, so we have chosen three representative and influential authors, Leon Kass, John Robertson, and Peter Singer, in part because of the diversity of their backgrounds (medicine, law, philosophy), in part because their ideas have been very influential, and in part because they come to different conclusions. This brief survey will hopefully illustrate the range of viewpoints of secular authors writing independently of any organized community.

Kass has become well known as an opponent of the new reproductive technologies (32). His main hesitation about them (beginning with artificial insemination and ending some day with ectogenesis) is that they divorce the genesis of human life from human sexuality and (ultimately) from the human body itself. This is a dehumanization of procreation, because it separates sex, love, and procreation, and should be resisted. But he has further hesitations as well. These include the following: (1) much of the new reproductive technology is viewed by Kass as a form of experimentation on the unborn and upon the parents, and while the latter can give consent, the former cannot. So we must be sure that risks to the unborn are minimal before these procedures can be justified; (2) in vitro fertilization usually involves early feticide on extra zygotes, and that raises a host of moral problems; (3) surrogate motherhood is a natural extension of the new reproductive technologies, and that involves all sorts of exploitation and/or psychological pressure; (4) the use of these techniques will lead to a new eugenic movement. Kass concedes that his position is not the most compassionate to those who suffer from infertility, although he reminds them of the possibility of adoption, but he believes that the above-mentioned problems argue for eschewing the use of in vitro fertilization and surrogate motherhood.

John Robertson's (57) point of departure is the well known Supreme Court decisions concerning contraception and abortion, decisions which he understands as giving women a right to decide not to conceive or not to bear a child already conceived. He believes that this needs to be broadened into a constitutional right to procreate in freedom, a right which would include the freedom to reproduce when, with whom, and by what means one chooses. This approach clearly places great emphasis upon the significance of the appeal to autonomy. For this reason, Robertson would extend the right to procreate in freedom to single adults as well as to married couples. Given the strong interests people have in reproductive freedom, the recognition of this right would mean that new reproductive technologies could at most be regulated when compelling state interests require such regulation. Regulations could not be justified because of purely moral considerations, absent a definite harm to some non-consenting individual. Moreover, according to Robertson, there is no justification for limiting their use to the treatment of infertility; people have a right to use them for the purposes of gender selection and for other types of selections.

It is obvious that Robertson's main concern is to argue against laws banning the use of the new reproductive techniques, while Kass's main concern is to argue for a negative moral evaluation of their use. One could in theory combine those two positions by accepting Kass's arguments about their immorality, while claiming that Robertson's arguments show that there is no justification for the legal banning of these techniques. This is not, however, Robertson's own position, since he explicitly rejects Kass's main argument about the dehumanizing unnatural aspect of the new reproductive technology.

Peter Singer's moral framework is a consequentialist framework, one which focuses on the potential consequences for individuals or for society as a whole of a new social approach. It is this framework which he (62) brings to bear on questions of the new reproductive technology, and which leads him to approve of non-natural technologies which employ human reasoning to attain human ends. It also leads him to reject many of the deontological arguments used against these technologies. Nevertheless, he feels that there are some serious issues even from a consequentialist framework concerning aspects of the new reproductive technology. He is concerned about the consequentialist advantages of altruistic over paid surrogates. He is concerned with where expensive techniques such as I.V.F. should fit into a national health care budget. But none of these concerns change his fundamentally positive appraisal of the new reproductive techniques.

There is no way to summarize the viewpoints of these scholarly bioethicists except to say that they approach the issues of the prevention and treatment of infertility from a variety of perspectives and reach important but radically different conclusions.

2. The Viewpoints of Feminist Writers

Any consideration of feminism as a single overarching set of principles and beliefs will be to some extent incomplete, as there are numerous versions of feminism. Nonetheless, there are certain general philosophical underpinnings of feminism, and to the extent that the various versions adhere to these, what follows reflects their position.

The main sources of information employed in this report about the teachings of feminism on the prevention and treatment of infertility are: (a) *Religion and Sexism*, edited by historian Rosemary Radford Ruether (58); (b) *Test-Tube Women: What Future for Motherhood?*, edited by three scientists, Rita Arditti, Renate Duelli Klein, and Shelley Minden (3); (c) *Making the Connections: Essays in Feminist Social Ethics*, by Christian feminist ethicist Beverly Harrison (26).

Feminism's foundation is the recognition that patriarchy and the subordination of women to men which have existed for millennia are wrong. Both involve an extension of mind-body dualism to male-female dualism, with the further claim that women are 'of the body' while men are 'of the mind'. Hence it has been asserted that men ought to lead, women to follow; men ought to dominate, women to submit.

The rejection both of dualism and its derivations constitutes the core of feminism. In particular, feminists reject the ideas that men and women are essentially different, that women are incapable of rational thought or autonomous action, and that men are inherently superior to women. These rejections have led, largely through appeals to their converses, to the articulation of a feminist ethic whose principles include: (1) justice based upon equal treatment of equals; (2) personal autonomy with freedom of choice; and (3) embodiment of reason. Of these, the concept of embodiment requires more detailed treatment. As a denial of the mind/body split, this principle radically opposes traditional ethics which have been based on appeals to revelation and/or reason, to the exclusion (in fact, to the denigration) of the body. Feminism insists that knowledge necessarily comes through the body; hence, sensual experience must be granted epistemic validity. Several imperatives derive from this emphasis: (1) The body will be both celebrated and respected as the foundation of personhood; (2) Mutual respect for persons must govern all interpersonal relationships; and (3) Only particular persons can properly determine what will be done to their bodies. These tenets have serious import for procreation generally and the new reproductive technologies particularly.

Feminists do not require that sexual activity leave open the potential for reproduction. In fact, insofar as motherhood limits choice, feminists often advocate contraception and, if that fails, abortion. Nonetheless, children may be desired by feminists, and for those freely choosing to have them, there is no feminist mandate against that choice. Feminists do, however, question how often the choice to have children is genuinely free, given a lifetime of exposure to a thoroughly patriarchal society and to male dominance which demands continuation of male lineage.

Clearly any projected manipulation of a person's body must be carefully scrutinized. Although there is nothing which in principle forbids the use of the new reproductive technology, feminists are reluctant to avail themselves of it for a number of reasons. First, insemination necessarily requires male participation. Still, for the woman who chooses to have a child but also to forego a male-assisted sexual encounter, artificial insemination by donor can enable her to have the desired child. Artificial insemination by husband would likewise be acceptable. Part of the acceptance of artificial insemination undoubtedly stems from the fact that it can be a do-it-yourself procedure. Instillation of sperm into one's own vaginal vault is relatively easy, and male friends (or anonymous carefully screened donors) may be willing to provide the sperm. This self-help method is often the treatment of choice by lesbians, as it keeps male participation to a minimum.

The second cause for feminist concern is that these methods have been developed by an almost exclusively male scientific community and supported by an almost exclusively male bureaucracy. Feminists charge that the scientific invasion is yet another way men take from women the control over their own bodies. Once again women must turn to men for fulfillment of their desires--for it is almost always a male scientist or physician who will technologically produce pregnancy.

In addition, feminists question the degree of refinement of the state of the art. They are not convinced that the technology has been sufficiently refined so as to be safe for the women who would use it. Moreover, they would certainly object to further refinements that perpetuated improper use of women as research subjects. These concerns, coupled with the suspicion that the motivation behind such research is to make women expendable, make them reluctant to use in vitro fertilization although, as stated previously, there is no in principle objection to the technique inself.

The same concerns drive an almost universal feminist rejection of surrogate motherhood, although again there is no in principle objection to surrogacy. If the motivating force behind a surrogate pregnancy is the continuation of the male lineage, the practice would probably be firmly denounced. On the other hand, if the request came from a woman who genuinely wanted but could not have her own child, feminists would not reject the possibility out of hand. The most prominent concern in this area regards the potential for abuse of women, i.e., a very real possibility that poor and minority women will be attracted, out of financial necessity, to participate in yet another form of procreative misuse, either as surrogate mothers or as host mothers following embryo transplant. The charge of misuse follows from the fact that, as the situation now stands, there is very little protection for surrogate mothers.

The following table summarizes feminist teachings on the prevention and treatment of infertility:

TABLE II. C2

(1) Infertility workups and medical and surgical treatments of infertility are suspect insofar as they are products of male-dominated fields and require the assistance of mostly male practitioners.

(2) A.I.D. and A.I.H. are morally acceptable and may even be advisable if and only if they are freely chosen, following informed consent, by the woman to be inseminated.

(3) In vitro fertilization is suspect insofar as it is the product of male-dominated research in which women subjects

have been abused, as the technique requires assistance of mostly male practitioners, and as its goals are suspect. Where these conditions do not obtain, the technique is morally acceptable if and only if it is freely chosen, following informed consent, by the woman involved.

(4) Surrogate motherhood is suspect insofar as it has vast potential for the abuse of all women, but especially of poor and minority women. Should surrogates be adequately protected and should pregnancy be undertaken for reasons not in conflict with feminist principles, it may be permitted.

3. The Viewpoints of Organized Health Professionals

Any discussion of the new reproductive technologies must take note of the viewpoints of the health professions. The opinions and concerns expressed by health care personnel are especially important, since they are among those most intimately involved in the development and application of such techniques.

The positions considered in this section will be those promulgated by the medical profession as a whole, of which the American Medical Association (AMA), the American College of Obstericians and Gynecologists (ACOG), and the American Fertility Society (AFS) are taken to be representative. Needless to say, individual practitioners may express dissenting views. The main sources of information employed in this section are: (a) *Current Opinions of the Council on Ethical and Judicial Affairs of the American Medical Association--1986* (14); (b) ACOG Ethics Committee Statement on *Ethical Issues in Human In Vitro Fertilization and Embryo Placement* (11); (c) Report of the Ethics Committee of the AFS on *Ethical Consideration of the New Reproductive Technologies* (18).

The AMA statements address only artificial insemination by donor (A.I.D.) and in vitro fertilization (I.V.F.). No reference is made to any substantive concerns about the acceptability of these techniques; rather, the focus is on procedural concerns (e.g. the need for informed consent and for donors' being carefully screened to preclude donations by persons with inheritable or infectious diseases). Thus, the AMA sees the new reproductive technologies as licit, but in need of judicious management of their application. Of interest is that the AMA apparently recommends that use of these techniques be limited to married couples. No mention is made of surrogacy.

The ACOG statement, like the AMA statements, reflects more procedural concerns than substantive concerns (although, in considering the treatment of embryos, a number of substantive issues are addressed). After noting that A.I.D. and I.V.F. can be supported by "strong and convincing ethical arguments," the statement turns attention to how best to insure success and minimize risk to the fetus and the mother.

In addition to whole-hearted acceptance of these techniques for married couples, ACOG extends their use to single persons, at the physician's discretion. The recommended bases for making these techniques available to singles are the "probable welfare of the resulting child and the avoidance of arbitrariness." Like the AMA, the ACOG makes no mention of surrogacy.

The AFS consideration of the new reproductive technologies is quite detailed. They consider each technique separately, and note both demonstrated (i.e., efficacy and safety well documented) and uncertain (i.e., further research on efficacy or safety required) indications, as well as rationales for and reservations about each. They find A.I.D., A.I.H., and

I.V.F. "ethically acceptable" when used for documented medical indications. Moreover I.V.F. using donor sperm, donor eggs, or donor embryos is acceptable within the constraints of medical necessity. Medical necessity is interpreted as meaning infertility of one or both partners desiring a child or as enabling single women to bear children.

The AFS does address the question of surrogacy, ultimately granting that there may be very limited application for its use, namely, when surrogacy is the only remaining option available to couples/women wishing children. However, the use of surrogate mothers for non-medical reasons (e.g., convenience to the biological mother) is not recommended. Moreover, the AFS continues to have serious ethical reservations regarding surrogacy; e.g., it worries about the possibility of psychological distress on the part of the surrogate mother, the eventual parents of the fetus, and the child as it grows up. Until more evidence is available, surrogacy must be considered clinically experimental and subject to the additional constraints of that status.

In summary, all professional groups surveyed consider at least some, if not all, of the new reproductive technologies to be morally licit; and all advocate their use in carefully circumscribed situations. Yet all share certain concerns and feel that utilization of these measures requires very careful monitoring. Seen to be especially central are the issues of confidentiality, informed consent, minimization of risk to mother and fetus, adequate screening of donors, appropriate handling of zygotes, and on-going evaluation of data obtained through the use of these techniques. Should further data indicate that these procedures are riskier or more productive of adverse results than is now believed, these groups might withdraw or further qualify their support.

D. Summary Table

We have presented an extensive set of data about the viewpoints of many traditions on different aspects of the prevention and treatment of infertility. Before proceeding with further analysis of that data, we need a summation of what we have so far discovered. The table presented below provides such a summation. It is important to keep in mind that such a summary table cannot capture many of the nuances in our earlier analysis, so readers of this report are cautioned to check earlier in the text for further explanations of the entries in this table.

There are several trends which emerge from a survey of this table. The first is the extent to which the Roman Catholic position which opposes nearly all techniques for the prevention and treatment of infertility is an extreme view with which no others agree. Nearly all of the traditions we have covered allow for the licitness of a fair number of the new techniques. The second is that the crucial issues for most traditions are the use of gametes from someone other than spouses and the treatment of all zygotes. These issues lead many to reject some of the techniques in question. Finally, surrogate motherhood is clearly the least acceptable of all of the techniques in question. We shall return to all of these points in Part IV of this report.

TABLE II.D

	TRADITIONAL INFERTILITY WORKUPS	A.I.H.	I.V.F. WITH SPOUSAL GAMETES AND NO ZYGOTE WASTAGE	A.I.D.	I.V.F. WITH NO RESTRICTIONS	SURROGATE MOTHERHOOD
Roman Catholic	I	I	I	I	I	I
Eastern Orthodox	A	A	I*	I	I	I
Anglicans	A	A	A	C	C	I
Lutherans	A	A	A	I*	I*	I
Reformed Protestants	A	A	A	C	C	I
Methodists	A	A	A	I	I	I
Mennonites	A	A	A	D	D	D
Baptists	A	A	A	C	C	C
Evangelicals	A	A	A	I	I	I
Seventh-Day Adventists	A	A	A	C	C	I
Christian Scientists	I	A	I	A	I	A
Jehovah's Witnesses	A	A	A	I	I	I
Mormons	A	A	A	C	I	I
Orthodox Jews	A	A	A	I	I	I
Conservative Jews	A	A	A	D	D	D
Reform Jews	A	A	A	A	A	A
Muslims	A	A	A	I	I	I
Professional Groups	D	D	D	D	D	C
Feminists	D	D	D	D	D	D

A = Accepted as Licit
C = Controversy about Licitness
D = Dependent Licitness (acceptable if right conditions are met)
I = Illicit
* = Considerable Potential for Change

Part III - PRESENT AND FUTURE IMPACTS OF THESE VIEWPOINTS ON INDIVIDUAL CHOICES AND ON COMMUNITY POLICY FORMULATION

B. Ways in which these Viewpoints can be Influential

Traditions do not make personal choices and do not determine social policies. Members of traditions do. We must keep this fundamental truth in mind when we examine the ways in which the viewpoints of the various traditions which we have studied can influence individual choices and community policy formulation. Traditions can influence these choices and these policy formulations only by influencing individual adherents.

There are many pathways by which this influence is exerted. Infertile couples who belong to a particular tradition may be aware of the viewpoint of their tradition, may accept that viewpoint, and may be led by that acceptance to make personal decisions in light of that viewpoint. Alternatively, they may seek the counsel of leaders of their tradition or of more knowledgeable friends or family members who also belong to their tradition, and those whose counsel they seek may lead the couple to accept certain treatments of their infertility and to reject other treatments. We need to keep these pathways in mind in the next section when we analyze the factors which are likely to determine the influence of a particular viewpoint on the decisions of individual infertile couples.

By whatever pathway a tradition exerts its influence on infertile couples, it will always have to struggle with the intense personal feelings of the couple seeking help with their infertility. This is less of a problem when a tradition influences public policy formulation. Societies formulate policies about the treatment of infertility when they decide about public funding for such treatment, about restrictions on or encouragements of various forms of research, about the enforceability of contracts, etc. In each of these policy decisions, individual members of particular traditions may be led, either by their personal knowledge of the viewpoint of their tradition or by the encouragement of leaders of their tradition, to adopt attitudes towards the policy decidings shaped by the viewpoint of their tradition.

It is clear then that there are many pathways by which the viewpoints of various traditions can influence individual choices and community policy formulation. Which of the traditions we have studied are likely to be more influential? How will this impact upon the use of the various techniques for treating infertility? We will attempt to answer these questions in our final summary. Before doing so, however, we first need to sketch an account of the factors determining the influence of various viewpoints.

B. Factors Determining the Influence of these Viewpoints

We should note at least three factors which will help determine the influence of various viewpoints: the size of the relevant community, the authority of the current viewpoints within the community, and the unanimity and diversity of opinion in the relevant community. Let us examine each of these factors separately.

1. The Size of the Relevant Community

The first relevant factor to consider is the size of the community in question. The larger the community, all other things being equal, the more there will be infertile couples whose individual treatment decisions are influenced by the viewpoints of that community. The larger the community, all other things being equal, the more there will be adherents who address public policy formulation in light of the viewpoints of that community. These reflections lead to the conclusion that our analysis must take into account the size of the relevant communities.

It is notoriously difficult to get accurate figures about the size of America's religious communities. The standard source is the *Yearbook of American and Canadian Churches*. It notes that some groups compile data annually and carefully, while other groups estimate membership every few years. Moreover, the definition of membership varies from one group to another. The figures to be presented below should therefore be taken as decent estimates rather than as firm figures.

It is estimated that about 60% of Americans belong to some established religious community. This represents about 140 million Americans. The following table provides a membership estimate for each of the traditions we have described (68):

TABLE III B.1

Roman Catholic Church	52,393,000
Southern Baptist Convention	14,178,000
United Methodist Church	9,405,000
Lutheran Churches	7,877,000
Mormon Church	3,602,000
Presbyterian Churches (Reformed)	3,122,000
Episcopal Church	2,795,000
Reform Jewish Movement	2,777,000
Muslims	2,000,000
Greek Orthodox Church	1,950,000
United Church of Christ (Reformed)	1,702,000
Conservative Jewish Movement	1,250,000
Orthodox Jewish Movement	1,000,000
Jehovah's Witnesses	650,000
Seventh Day Adventists	624,000
Mennonite Churches	110,000

We have provided no figures for the Christian Science Church, which refuses as a matter of policy to publish membership figures, for the evangelical tradition, which cuts across so many other groups that an accurate count is not possible, and for the various secular traditions that lack an organized structure that makes a membership figure meaningful.

2. The Authority of the Current Material

The second relevant factor to consider is the authority of the material and viewpoints we have identified within the community in question. The more authoritative the material, all other things being equal, the more there will be infertile couples whose individual treatment decisions are influenced by these viewpoints. The more authoritative the material, all other things being equal, the more there will be adherents who address public policy formulation in light of the viewpoints of that community. These reflections lead to the conclusion that our analysis must take into account the authority of the material and the viewpoints we have identified within the community in question.

At one extreme are communities which emphasize the importance of individual judgments. These include religious communities such as the Baptists and the Evangelicals as well as secular traditions such as the tradition of individual scholars and the feminist tradition. At the other extreme are traditions and communities with centralized teaching authorities such as the Roman Catholic Church. In between are communities which formulate general policies at organized centralized meetings but which see these policies as reflections of current thinking rather than as authoritative teachings. These include the decisions of the General Convention of the Episcopalian Church, the General Assembly of the Presbyterian Church, and the General Conference of the United Methodist Church. Also in between are communities which emphasize the authority of leading religious scholars, while recognizing that these scholars may disagree. These include the Muslim community and the Jewish community.

It is difficult to rank the material we have analyzed in Part II of this report by degree of authoritativeness within the community in question, but the following table represents our best estimate of the degree of authoritativeness of the material we have analyzed:

Table III B.2

MOST AUTHORITATIVE	IN BETWEEN	LEAST AUTHORITATIVE
Roman Catholic	Anglican	Methodist
Eastern Orthodox	Lutheran	Baptist
Jehovah's Witnesses	Reformed	Evangelical
	Mennonite	Seventh-Day Adventist
	Jewish	Christian Scientist
	Muslim	Secular
	Mormon	

3. Unanimity and Diversity of Opinion in the Relevant Community

The final factor to consider is the unanimity and diversity of opinion in the relevant community. The greater the diversity of opinion, all other things being equal, the less constrained individual infertile couples will feel when confronting choices about particular treatment decisions. The greater the diversity of opinion, all other things being equal, the less the community in question will be able to influence public policy decisions. These reflections lead to the conclusion that our analysis must take into account the unanimity and diversity of opinion within the relevant community.

There is little point to restating the extent of diversity of opinion in particular communities discovered in Part II of this report. We will return to this factor in our final summary section.

Part IV - SUMMARY AND CONCLUSIONS

This final part of our report brings together all of our results and attempts to draw some conclusions about the likely impact of all of these viewpoints on the future of the prevention and treatment of infertility in the United States. It will be divided into four sections, each focusing on one major type of intervention.

A. Traditional Workups and Medical and Surgical Interventions

The traditional infertility workup begins with both individuals undergoing a history and physical and certain lab tests (e.g., serologic test for syphilis, complete blood count, urinanalysis, serum level of thyroid stimulating hormone as measured by radioimmunoassay). The man is then scheduled for several semen analyses, with the specimens obtained either by masturbation or by coitus interruptus. The woman is scheduled for a series of tests (e.g, a hysterosalpingogram, a postcoital test, a serum progesterone or an endometrial biopsy) timed around her cycle. Then, depending upon the cause of infertility, medications (e.g., hMG, hCG, progesterone, clomiphene citrate) or surgical interventions (e.g., repair of hypospadias, tubal resection and anastomosis) are ordered.

Most of the traditions we studied found these techniques completely acceptable. That is, in fact, an understatement. A large number of the traditions believed that such treatments of infertility are very desirable, in part because they help meet important personal needs and in part because procreation is viewed as having considerable religious significance. There is little controversy about this support and it grows out of some of the most authoritative teachings of these traditions. Consequently, one can expect that members of these traditions facing a personal problem with infertility will choose to undergo such traditional workups and interventions and that members of these traditions will support public policies encouraging the use of these workups and interventions.

We found only three traditions which had significant hesitations about these traditional techniques. Christian Scientists, as part of their general philosophy of alternatives to traditional health care, would oppose the use of the drugs and the surgical interventions in these traditional techniques. Feminists object to these traditional techniques when the desire for children grows out of a male-dominated choice which demands continuation of the male lineage, but would find them acceptable when they are freely chosen by both parties. Finally, the Catholic Church has substantial objections to the masturbation involved in the infertility workup. Of these three concerns, the last is the one likely to have the greatest impact because it arises out of authoritative teachings in a large community. Nevertheless, there are reasons for expecting that the impact will not be that great. As noted in Section II B.1, many Catholic theologians have in recent years argued for the licitness of such techniques as long as they are intended to lead to reproduction within conjugal bonds. Moreover, it has been widely reported that individual Catholics have dissented from the teaching of the Catholic Church about the need to combine conjugal sexuality and reproductive potential in each sexual act.

In short, then, our analysis suggests that there would be widespread enthusiastic support for these traditional techniques and even more widespread acceptance of their moral licitness. While a few traditions have hesitations about their use or actual grounds for opposing their use, that hesitation and/or opposition is not likely to be influential. The following table summarizes these conclusions:

TABLE IV.A

TRADITIONS ENCOURAGING USE	TRADITIONS WHICH ACCEPT USE	TRADITIONS WITH HESITATIONS	TRADITIONS WHICH OPPOSE ELEMENTS
Eastern Orthodox	Anglican	Feminist	Christian Scientist
Lutheran	Methodist		Roman Catholic
Reformed	Mennonite		
Southern Baptist	Seventh-Day Adventist		
Evangelical	Jehovah's Witnesses		
Mormon	Professional Groups		
Jewish			
Muslim			

B. Artificial Insemination

There are, of course, two major forms of artificial insemination. A.I.H. uses sperm from the husband. It is unequivocally indicated and quite effective when semen analysis is normal and when the cause of infertility is the anatomic inability of the male to place sperm against the cervix. It may be effective in cases of abnormalities found in semen analysis or in postcoital testing, and its effectiveness in such cases is increased when procedures are used to increase the number of sperm delivered to the cervix, to eliminate agents in the semen which are noxious to the sperm, and to bypass inhospitable cervical mucus. A.I.D. is used in other cases of male abnormality or in cases where the male is a carrier of a dominant genetic abnormality.

Our survey found that most traditions do not treat these two forms of artificial insemination as morally analogous. While Roman Catholicism is the only tradition with intrinsic objections to the use of A.I.H., many traditions objected to or had serious doubts about the licitness of A.I.D.

Even Roman Catholics had greater objections to A.I.D. than to A.I.H. So these two techniques need to be treated separately.

The Roman Catholic opposition to A.I.H. is based upon the belief that individual acts of procreation must grow out of individual acts of conjugal sexuality. This is the other side of the Roman Catholic opposition to contraception, which is based upon the belief that individual acts of conjugal sexuality cannot licitly be deprived of their reproductive potential. None of the other traditions insist upon this connection. At most, they believe that individual acts of procreation must grow out of conjugal sexuality but need not be the result of a particular act of conjugal sexuality. And, as noted before in Section IV. A, there is considerable opposition both among Roman Catholic theologians and among Catholic laypeople to this special doctrine, so there is some question about how influential this viewpoint will be, despite the authoritativeness of its source and despite the size of the Roman Catholic community.

A.I.D. is a very different matter. It involves the introduction of genetic material from someone other than a spouse, and this leads a number of additional traditions to oppose it or to hesitate about its use. Some reject it as a form of adultery, some reject it because it involves procreation not growing out of conjugal sexuality, and some reject it because it involves a confusion of lineage. The communities which definitely reject A.I.D. include the Eastern Orthodox Church, Orthodox Judaism, Islam, some Protestant groups (most Lutherans, Methodists, and Evangelicals) and the Jehovah's Witnesses. Other communities are concerned about these arguments but are still not sure about their final view and/or are badly split over their final view. These include the Anglicans, the Presbyterians, the Baptists, the Seventh-Day Adventists, and the Mormons. Only a small number of communities clearly support A.I.D. Those who support A.I.D. do so either because (and just when) the use of A.I.D. is a freely chosen loving decision made by both spouses as an expression of their love for each other (e.g., the Mennonites, those segments of the above mentioned Protestant groups favoring A.I.D., and Conservative and Reform Judaism), or because they support individual procreative autonomy (e.g., several of the independent secular and/or professional scholars and the feminist movement). The crucial difference between the two groups is whether they support A.I.D. for single women desiring to have children. Of particular interest in this connection is the strong support of segments of the feminist community for A.I.D. for single (sometimes, but certainly not always, lesbian) women.

In short, then, our analysis suggests that there would be widespread acceptance of the moral licitness of A.I.H., considerable hesitation about the moral licitness of A.I.D., and even less support for the use of A.I.D. by single women. The following table summarizes these conclusions:

TABLE IV.B

TRADITIONS OPPOSING ALL ARTIFICIAL INSEMINATION	TRADITIONS SUPPORTING A.I.H. ONLY	TRADITIONS SPLIT OVER A.I.D.	TRADITIONS SUPPORTING A.I.D. IN THE CONTEXT OF A MARRIED COUPLE	TRADITIONS SUPPORTING A.I.D. FOR SINGLE WOMEN
Roman Catholic	Eastern Orthodox	Anglican	Mennonite	Feminist
	Lutheran	Reformed Protestant	Christian Scientist	Some Secular and Professional Scholars
	Methodist	Baptist	Conservative and Reform Jewish	
	Evangelical	Seventh-Day Adventist		
	Jehovah's Witnesses	Mormon		
	Orthodox Judaism			
	Muslim			

C. In Vitro Fertilization

In vitro fertilization has emerged as a reasonably successful technique for treating women with tubal obstructions. Multiple follicular maturation is induced, oocytes are recovered through suction guided by laparoscopy, fertilization takes place in a special medium, and the fertilized eggs which reach the 4-cell level are transferred by use of a catheter to the endometrial cavity.

Providing that only spousal gametes are used and that all zygotes are transferred back to the endometrial cavity, there are few traditions which treat I.V.F. as raising special problems. The only two are the Eastern Orthodox and the Christian Science traditions. Eastern Orthodox opinion, following ideas expressed by Paul Ramsey and Leon Kass, finds the use of I.V.F. as too dehumanizing and as excessively separating reproduction from conjugal sexuality. Christian Scientists, who have no objection to A.I.H., oppose I.V.F. because of the use of medicines and surgical techniques.

The situation becomes very different when I.V.F. involves donor gametes and/or when not all zygotes are reinserted in the hope of implantation. The former raises a problem for all those traditions who oppose A.I.D. (Lutheran, Methodist, Jehovah's Witnesses, Evangelical, Orthodox Jewish, Muslim) or who find A.I.D. controversial (Anglican, Reformed Protestant, Baptist, Seventh-Day Adventist). The latter raises a problem for all those traditions who strongly oppose abortions from the moment of conception (especially Catholic, Eastern Orthodox, Mormon, Jehovah's Witnesses).

All of this suggest that there is likely to be almost as much support for I.V.F. as for A.I.H. so long as only spousal gametes are used and so long as no zygotes are wasted. Support lessens to some degree when there is zygote wastage and to a much greater degree when donor gametes are employed. The following table summarizes the results of this analysis:

TABLE IV.C

TRADITIONS WHICH INTRINSICALLY OPPOSE I.V.F.	ADDITIONAL TRADITIONS WHICH OPPOSE IT WHEN THERE IS ZYGOTE WASTAGE	ADDITIONAL TRADITIONS WHICH OPPOSE IT WHEN DONOR GAMETES ARE USED	TRADITIONS WHICH APPROVE
Roman Catholic	Mormon	Lutheran	Mennonite
Eastern Orthodox	Jehovah's Witnesses	Methodist	Conservative and Reform Jewish
		Evangelical	
Christian Science		Orthodox Jewish	Secular and Professional Authors Feminist
		Muslim	
		Many Anglicans Reformed Protestants Baptists and Seventh-Day Adventists	Other Anglicans Reformed Protestants Baptists and Seventh-Day Adventists

D. Surrogate Motherhood

Surrogate motherhood involves using a husband's sperm to artificially inseminate a woman other than his spouse. That woman carries the fetus until birth, at which time it is adopted by the spouse. The surrogate is usually paid a fee for that lengthy service. When it was first introduced, I.V.F. had not yet been successfully employed, so most of the early cases involved women with blocked tubes. This is still true in some cases of surrogacy, even though such cases can now be treated by use of I.V.F. Full surrogacy is required primarily in cases in which the wife has neither usable gametes nor a competent uterus. Women with usable gametes but without a competent uterus can contribute those gametes for use in I.V.F. where the zygote will be implanted into another woman, the gestational surrogate.

We need to distinguish the moral analysis of full surrogacy from the moral analysis of gestational surrogacy. Independent of any special moral concerns about surrogacy, traditions opposing A.I.D. will also oppose full surrogacy, while traditions intrinsically opposed to I.V.F. will be intrinsically opposed to gestational surrogacy. There are, however, many additional concerns which have been raised about surrogacy itself. These include: concerns about whether this constitutes a form of illicit baby-selling, concerns about the exploitation of surrogate mothers who may need the fee, concerns about harmful effects to all parties involved (e.g., the disruption of the bonding between the infant and the gestational mother), concerns about the possible depersonalization of motherhood, and concerns about possible confusion of lineage.

These many concerns help explain why few traditions support surrogate motherhood. Some secular thinkers who emphasize procreational autonomy and freedom of contract argue for its licitness if all parties freely consent. A few religious thinkers (notably but not exclusively biblical theologians who are influenced by Old Testament patriarchal accounts regarding the importance of preserving male lineage) join in guarded approval. But these are exceptions, and the formulation of public policy in this area needs to keep this in mind.

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RISKS OF INFERTILITY DIAGNOSIS AND TREATMENT

A Report

submitted to

THE OFFICE OF TECHNOLOGY ASSESSMENT

July 11, 1987

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RISKS OF INFERTILITY DIAGNOSIS AND TREATMENT

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RISKS OF CERVICAL MUCUS EVALUATION

I have been unable to find any hazards of cervical mucus evaluation, unless one considers false positives or false negatives a hazard. If such false information meant that AID (for example) would be scheduled at a time unlikely to result in pregnancy, then the infertile woman would subject herself to the risks of AID more times. [See AID.] Furthermore, a mistake in finding an ovulatory mucus pattern when it actually exists (false negative) might mean that a woman would be needlessly enrolled in one of the more hazardous treatments described in this report. Graham et al have shown that instruction in charting cervical mucus has (coincidentally?) led to pregnancy in 17.7% of couples who were unable to conceive for at least one year (1).

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RISKS OF ENDOMETRIAL BIOPSY

SUMMARY

Sampling the endometrium to assess its condition during the luteal phase of the menstrual cycle puts a patient at certain risk of pain, bleeding and uterine cramping. Uterine perforation is a hazard. If she is pregnant, abortion may occur, although some embryos do survive endometrial biopsy. Some authors list endometrial biopsy as a possible cause of iatrogenic infertility.

INTRODUCTION

Endometrial biopsy (EB) is a painful procedure in which samples of the uterine endometrium are extracted from two to four sites. In the infertility investigation it is used to 'stage the endometrium,' i.e., to assess whether the candidate has luteal phase defect (LPD)(3,12), or to monitor whether fertility drug treatment has rectified LPD (3). The cervix is grasped with a tenaculum and an interuterine sound is introduced (3). Local anesthesia (e.g., lidocaine) may be used. Once the cervix is adequately dilated, a curette or aspirator is passed to the uterine fundus. Usually samples are taken in 4 quadrants (3).

Several aspects of the use of EB in infertility diagnosis are controversial (11,12). One question is whether EB detects LPD better than serum progesterone (P) determinations do (1,2,9). Expense comes into this debate, for some consider the P assays more expensive (2), others, the EB (9). A second question is whether one gets an unacceptable percent of false positives, i.e., when the endometrium is falsely diagnosed as out-of-phase. Several investigators repeat the biopsy (when patients permit it) if the initial results show out-of-phase (1,12). After second biopsies, Wentz et al. reported that first biopies had 29% false positives (10), and Wild et al., that they had 43% (12). Such figures make one doubt the second 'positive' results also. Also controversial are what type of sampling device to use, patient acceptance, morbidity, and risk of pregnancy interruption.

RISKS

The side effects that are usually mentioned to patients are uterine cramping and light bleeding for several days (3). Some clinicians use prostaglandin synthetase inhibitors to reduce uterine cramping (12). A paracervical block may be used if there is cervical stenosis (3).

Pain: Extreme pain is reported in the lay literature (6). The fact that most investigators who wish to do a second biopsy meet patient resistance is evidence to me that there is considerable pain during and/or after EB (4,9, 12). In south central United States 56% of 263 candidates would not permit a repeat (12). Compliance in Barcelona Spain is more complete, for Balasch reports that his use of the Semm suction-curette is painless (2). In Montreal Ferenczy got no refusals of a repeat test when he used the Endocyte disposable plastic brush, and 60% refusal of a true biopsy (4).

Puncturing the uterus is another risk; this has not been reported during infertility investigations, but during biopsies for suspected cancer (8).

Clinicians mention interruption of pregnancy as a risk of EB in infertile women. EB to assess luteal phase endometrium must be done just a few days before menstruation starts; thus a woman could be pregnant. In a series of 1,174 EBs, Wild et al. found 27 pregnancies (12). In one case, the actual blastocyst was removed by the curette; in another abnormal bleeding and hematoma formation resulted in an early spontaneous abortion; four other women aborted spontaneously. The authors conclude that six abortions (22%) is about the usual incidence among infertility patients (12).

The bottom line is whether endometrial biopsy actually helps cure infertility. Indeed, some gynecologists call EB an iatrogenic cause of infertility (5,7).

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RISKS OF ULTRASONOGRAPHY IN INFERTILITY TREATMENT

SUMMARY.

In infertility treatments, realtime ultrasound may be used in oocyte retrieval, artificial insemination, and embryo transfer; and diagnostic ultrasound is regularly used for monitoring follicle size during hyperstimulation and early pregnancy after ET. In extensive studies of ultrasound screening later in pregnancy, no serious hazards have been found. Risks of infertility ultrasound might be: adverse effects on the corpus luteum; defective implantation of the blastocyst; developmental defects; endometrial damage; premature ovulation; morphological damage to the ovary; and disturbed meiosis in oocytes. Hyponatremia is an incidental hazard. Appropriate studies are not being done to assess mid-term and long-term risks.

INTRODUCTION.

Ultrasound (US) is used in medicine in four ways (45): 1) for surgery, by focussing a beam of high-frequency inaudible sound waves to cut tissue; 2) for therapy, by creating heat or mechanical disruption in the tissue or organ at which it is directed; 3) for 'real-time' imaging, by visualizing an instrument inserted into the body as it performs some therapeutic action, and 4) for diagnosis, by visualizing an internal problem. As far as I know, methods 1 and 2 are not used in infertility treatments, so I direct my attention to the other two.

US is non-ionizing radiation, that is, it does not knock out electrons when it hits matter. (However, generation of free radicals has been demonstrated (4).) It is therefore not expected to cause chromosome changes leading to mutations or activation of oncogenes (cancer genes). It can be continuous or pulsed. Strength is measured in watts per square centimeter;

for pulsed waves there are several possible ways of calculating strength, two common ones being I(SATA) = spatial average/temporal average, and I(SPPA) = spacial peak/pulse average (14). It is difficult to measure strength as the US leaves the transducer, and more difficult as it penetrates tissue because of the scattering effects of different types of tissues (25,33). Machines in the past have been poorly calibrated (37), and determining optimum exposure conditions is difficult (33,34,44). Another problem is that low frequency US cannot pass through air, and water is better than solid tissue. Abdominal sonography works best, then, through a full urinary bladder. Risks from US could come from: excessive heat where it was not intended; cavitation (the forming of gas bubbles that resonate with the waves of US); and other mechanical stress (6,44). The bioeffects committee of the American Institute of Ultrasound in Medicine has reported that, "In the low megahertz frequency range, there have been no independently confirmed significant biological effects in mammalian tissue exposed to intensities below 100 mW/cm^2" (6). [W = watts] The I(SATA) 10 mW/cm^2 has also been suggested as a limit (34).

REAL-TIME ULTRASOUND.

In the infertility 'treatment' IVF/ET, 'real-time' sonography may be used during ovum pick-up instead of laparoscopy in the several methods of 'nonsurgical' ovum pickup (also called 'ultrasonically directed'). [See section ULTRASONICALLY DIRECTED OOCYTE RETRIEVAL for references and description of methods.] Ultrasound transducers may be placed in various locations on the abdomen or in the vagina. Because visualization is much improved with the transducer in the vagina, this method has become popular; since September 1985 several firms have marketed vaginal transducers (46).

Real-time sonography may be used in AID and IUI (11) and in a new method of embryo transfer by injection directly through the abdomen (13,36,44a).

During ovum pick-up, the ovary is the organ that receives the most US: interstitial and follicular cells, ripe ova (in metaphase II) and immature ova (in the diplotene stage). In embryo transfer, again the ovary, because it will often be in the path of the beam, also receives US, as well as the very early embryo. Since, however, the main recipients of US in DIAGNOSTIC sonography used in IVF/ET are likewise the ovary, the ova, and the embryo, risks of real time ultrasound are discussed under "Diagnostic US," below.

DIAGNOSTIC ULTRASOUND.

In IVF/ET, diagnostic US is used in two main ways: (a) during ovarian hyperstimulation, to judge follicle size in order to time injections of hCG (17a), and (b) after ET, to monitor the first few weeks of potential pregnancy to watch for ectopic pregnancies and to determine whether implantation has occured. In the first, the ovary with its current and future mature ova are targets; in the second, the ovary, the endometrium, and the early embryo. After ET, the ovary should have a functioning corpus luteum: therefore, two additional questions are whether previous ultrasound has impaired corpus luteum formation, and whether concurrent ultrasound affects it now. This concern is added to those about risks to ova and the early embryo.

PREVIOUS STUDIES ON RISKS OF OBSTETRIC ULTRASOUND.

The vast bulk of the literature on the risks of 'obstetric' US does not consider irradiation of ovaries, oocytes, endometrium and corpus luteum. 'Early' diagnostic ultrasound in obstetrics generally refers to the period at about 16 to 18 weeks of pregnancy, and 'late' to the period 32 to 33 weeks (27,32). Thus 'early' is well past the stage of most organogenesis when the notorious teratogens are known to act. Truly 'early' use of diagnostic ultrasound, i.e., in the first trimester, is usually only with patients who have been treated for one or another infertility problem.

Recently several national and international seminars, hearings, and symposia have considered obstetric US (as defined above); most conclude that there are no obvious and clearly evident short-term or mid-term hazards of diagnostic US, either to mother or child. The United States National Institutes of Health held a consensus development hearing in 1984 on "Diagnostic Ultrasound Imaging in Pregnancy"; although no serious hazards were confirmed, they concluded that routine screening of all pregnant women cannot be justified (30). Somewhat similar conclusions were reached at a Scientific Group Meeting of the World Health Organization in September 1984 (19). At about the same time the Royal College of Obstetricians and Gynaecologists' working party concluded, in contrast, that routine screening could be encouraged (37). The Royal Society of Medicine held a Forum on Maternity and the Newborn in April 1985; many of the particpants there raised concerns about efficacy and safety (27,32,38,43). The College of Radiographers met at London Hospital, also in April 1985 (15), and the World Federation for Ultrasound in Medicine and Biology met in Sydney in July 1985: discussants in a special symposium concluded that there was no evidence of adverse effects of US on mother or fetus (48).

See Section II for comments on studies of effects on children of US exposure in utero.

As far as I know, women who have received US while pregnant have not been surveyed. Gross adverse effects presumably would have been noticed. However, despite reports of women's bonding to the US images of their progeny and of women's enthusiasm for sonography, negative reactions have been recorded: some women have been frightened by insensitive operators, lack of information provided and hints of something sinisterly wrong (26,43).

It is interesting that in the above-listed seminars, hearings, and symposia, the only two that included in their conclusions doubts about the value of US and concern about hazards were those that permitted considerable consumer input. The U.S. N.I.H. consensus development hearing had a strong presence from the National Women's Health Network (30); the Royal Society of Medicine's forum had delegations from consumer groups, for example, the Association for Improvements in the Maternity Services (AIMS) (27,32,38,43).

RISKS PERTINENT TO SPECIFIC USES OF ULTRASOUND IN INFERTILITY TREATMENTS.

1) The corpus luteum: Possible adverse effects on the corpus luteum have not, as far as I know, been looked at directly. There is a low rate of pregnancy completion in IVF and often as many as 1/3 of all transferred embryos may fail to get as far as even a 'biochemical' pregnancy. Several factors might be responsible for this -- probably more than one factor acts, perhaps synergistically -- but it could be that ultrasound has damaged the corpus luteum. 'Luteal phase defect' is a recognized condition and is prophylactically treated in many clinics by progesterone or hCG. [See section on fertility drugs.]

2) The early embryo might be damaged so that it cannot implant properly -- damaged by US as it is being transferred into the uterus, or in the next few weeks when the beginning of pregnancy is monitored with US. The embryo might acquire a defect leading to a spontaneous abortion, to stillbirth, or to a disabled child. Essentially no experimental works relates to this (5). Barnett has found no effect of US on development in 18-hour chick embryos, the stage most sensitive to US (3), and Sikov's own experiments and in-depth

review of the literature reveal no deleterious effects of US exposure in mammals, except for heat effects at dosages well above those clinically relevant (40).

3) The endometrium of the uterus might be affected in such a way as to make it less receptive to placentation. See comments under 1) above.

4) Follicles might be stimulated to rupture before ova were mature (44b). In mouse ovaries US has caused morphological damage (2); also Demoulin et al. obtained fewer rat fetuses when mother rats' ovaries had been exposed to US (11). In Demoulin's work with human superovulation and AID, fewer pregnancies were established when ovaries were monitored by US (11). Or ovarian tissue could be damaged in such a way that a future pregnancy would be less likely: i.e., an iatrogenic effect in which infertility treatment could make a subfertile woman actually infertile. There have been some hints at this in the literature (35). If US does indeed compromise the establishment of pregnancy, the effect may belong under categories 1),2),3), 5), or 6).

5) Oocytes in metaphase II could be damaged so that they do not complete the second meiotic division properly. There could be sister chromatid exchanges (SCE) or nondisjunction leading to aneuploidy. IVF embryos that fail to divide normally often do show chromosome abnormalities.

The reasonably voluminous literature on whether US can cause SCEs does not draw unequivocal conclusions; since Miller has reviewed it thoroughly (24), I shall summarize it only sketchily here. Many published studies have been poorly designed and do not use a positive control, i.e., a control group treated with an agent that always creates SCEs, such as mitomycin (24). Sometimes SCEs are not scored blind: measurement of SCEs, with one of the sister chromatids radioactively labeled, is quite subjective. Some studies with positive results could not be repeated by other investigators (4,9,10, 20,25). Nevertheless the question is still moot (23).

Most of the studies reviewed by Miller have not described effects of US on meiotic cells. However, Moutshen demonstrated deleterious effects of US on male rat testes (28), but Williams et al found that US during preovulatory meiotic maturation of the rat oocyte did not affect the rats' reproductive performance (47).

6) Oocytes in diplotene might be damaged. One way to test this would be to tabulate establishment of pregnancies and miscarriages in a second cycle after a first one using extensive US. Most clinics do report lower success rates in second, third, and fourth attempts at IVF, but a myriad possible factors could cause this.

NECESSARILY INCIDENT HAZARDS OF ULTRASOUND.

One hazard in US use is the full bladder. Not only do IVF patients frequently complain of the pain and stress, but excessive water drinking can itself be life-threatening. Two serious cases of hyponatremia in geriatric patients after pelvic sonography have been reported (8,17). That practioners are themselves concerned about patients' discomfort and borderline hyponatremia at a time when stress should be avoided is shown by the many enthusiastic endorsements of the vaginal transducer which does not require a full bladder.

The threat of hyponatremia needs to be emphasized. As far as I know, this has not been investigated as a contributory factor in the deaths from IVF. In Arrief's study of 15 women under age 42 who died or remained permanently comatose from hyponatremia after elective surgery, seven had had gynecological surgery (1). It is true that some had been taking sodium-depleting drugs, and most had received post-surgery analgesics that also tend to lower sodium. However, Arrief discusses the fact that more women than men die from hyponatremia and that possibly sex hormones influence the sodium-potassium pump in the brain. Since the sex hormone balance has been altered considerably in IVF candidates, they may be at particular risk for hyponatremia. A further distressing factor is that there is no sure method of correcting sodium balance after severe hyponatremia (1).

DISCUSSION.

We do indeed have effects in IVF with unknown causes: ova that do not fertilize, chromosome aberrations that apparently prevent early cell division, a very poor record of successful implantation. It is unlikely -- but possible -- that US affects one or another of these. (Far more likely would be that this low success arises from fertility drugs or from the cause of the patient's infertility.) One test would be to see if any of these adverse effects diminishes when no US is used. However, in the early days of IVF US was not used, and success was similarly very low. Now ultrasound is almost universally used to monitor follicle growth, even if not for other purposes; probably no practitioner would want to give up its usefulness in the hope of a small increase in success rate.

Poor success rates, indeed, cannot be considered a 'risk,' since both patients and practitioners — aware of its low success — have accepted IVF.

Dunn from the Bioacoustics Research Laboratory at the University of Illinois has stated: "there are no short-term effects of diagnostic ultrasound in humans since none have been reported... following more than 20 years of rather intense medical employment .." And further, "any long-term effects that may occur will not be observed as they are not being sought by appropriately designed programs" (12).

To an extent these conclusions can apply to the uses of ultrasound in infertility treatment. First, one can never 'prove' a 'no harm' hypothesis. Second, most of the studies on hazards have been done by radiologists or obstetricians, neither of whom can be considered unbiased. Third, ultrasound gives so many obvious advantages over previously used methods (for example, in finding follicles ready to ovulate, instead of just using LH hormone level in the blood, and in directing ovum pickup without the hazards of laparoscopy) that practitioners and patients might well be prepared to accept disadvantages.

Dunn's challenge is the appropriately designed experiment. Most of the effects about which I speculate above could be caused by other factors. Which ones ought to be isolated for study? Then, what study will treat human subjects fairly while at the same time testing the tool of ultrasound that is now an integral part of the IVF protocol? US is unequivocally more essential to IVF than it is to normal obstetrics, where it is now also integral.

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RISKS OF HYSTEROSALPINGOGRAPHY

SUMMARY.

The technique of hysterosalpingography -- visualization by an X-ray opaque dye of the uterus and fallopian tubes -- raises controversies over choice of dye, when its use is appropriate, side effects, and pain. Risks include: intravasation, granuloma, pain, false positives and false negatives, radiation damage, adhesions, and pelvic inflammatory disease. An almost universal part of the infertility 'workup,' the painful HSG occasionally brings about an immediate pregnancy and usually diagnoses tubal problems, but it can also cause infertility.

INTRODUCTION.

Hysterosalpingography (HSG) is the X-ray visualization of the fallopian tubes after injection of a radio-opaque dye, a contrast medium (3). Current HSG also includes 'hysterography,' visualization of the uterus. Contrast media may be water soluble (WSCM), such as Renographin, or oil-soluble (OSCM), such as Lipiodol and Ethiodol. The patient may or may not be given an analgesic or tranquilizer; the cervix is usually grasped with a tenaculum and the dye injected through the cervix. The passage of the dye and the shape of the uterus and fallopian tubes are monitored with X-rays or, more usually, with fluoroscopy. Although a diagnostic tool, the procedure, for unexplained reasons, sometimes has a therapeutic effect. If at least one tube is patent and the patient is ovulatory, most practitioners give her six months in which to become pregnant without further treatment.

Three controversies in the current medical literature are: 1) OSCM versus WSCM (15); 2) the contemporary place of this technique -- compared with modern laparoscopy -- in infertility treatment (2,11); and 3) pain control.

1) The older medical literature and some recent papers report that OSCM is more therapeutic than water (9), but most workers believe that it is more painful than WSCM, with more danger of intravasation and/or granulomatous inflammation in the tubes. However, Alper et al in a randomized prospective study with 106 patients demonstrated the same subjective rating of pain for each medium, the same pregnancy rate, and no granuloma. There was indeed more intravasation with OSCM, but no morbidity resulted from this (1). Alper recommends that one choose OBCM for better contrast or WBCM for demonstrating tubal mucosa.

Bateman et al also demonstrate the safety of OBCM and recommend Ethiodol (a low-viscosity poppy seed oil with 37% iodine). Deaths after OBCM all occured before 1948 when the more viscous Lipiodol was used (2). DeCherney prefers to use both WSCM and OSCM in most patients (7).

2) Bateman et al strongly recommend both HSG and laparoscopy as being useful and complementary in modern gynecology (2). However, Rice et al are more critical in their 1986 review of HSG. With 143 patients who had both HSG and laparoscopy with chromotubation (methylene blue injected through the cervix), they found that tubal patency was not accurately demonstrated with HSG. They got 15.9% false positives and 14.9% false negatives for tubal patency. Only 17% of the HSGs demonstrated uterine pathology that would have been missed with the laparoscopy, whereas 76% of the laparoscopies picked up unsuspected intraperitoneal disease (12).

3) Control of pain is a minor issue. Some clinicians give no medication of any sort (1)(2); Sheikh gives atropine and analgesics (14); Rice gives Demerol (12); rarely local anaesthesia is used around the cervix.

RISKS.

1) Intravasation. Only one death has been reported since 1947. Before that date deaths occured after use of Lipiodol, from intravasation in veins in the fallopian tubes or uterus, with oil moving to cause an embolism in the lungs. Intravasation can also occur in the lymphatics. Currently clinicians believe that no serious intravasation can occur with the use of Ethiodol. When Bates saw intravasation on the fluoroscope (2.4% of his patients), his team stopped injection immediately, and did chest fluoroscopy. They found no oil in the chest and no morbidity of any sort resulted (2). Symptoms of oil embolism would include pain in the chest, tachycardia, and cough.

2) Granuloma. Because OCSM may remain in the fallopian tubes for days, some workers consider this a serious hazard (4). To avoid granuloma, Beyth et al. flush the uterine cavity with Hartmann's solution and perform tubal surgery, if indicated, soon after the HSG (5). DeCherney uses first WSCM, followed by OSCM only if the tubes are normal (8,9).

3) Pain. The lay literature has some vivid descriptions of the excruciating pain of HSG (6), but many clinicians use no medication. Sheikh shows considerable concern and comments on the difficulty of working with frightened patients (14). After giving demerol, Rice got no complaints of pain (12). Bateman believes that injecting the dye with very little pressure avoids pain (2). And Alper's 106 patients gave an average response of 3 when asked to rank their pain, with 0 representing no pain and 5, severe pain (1).

4) False Positives and False Negatives. If other workers, like Rice (12), get about 15% in each of these categories, then patients are at a rather considerable risk of being treated for occluded tubes when not necessary, or being scored as 'idiopathic' infertility when blocked tubes are the cause.

5) Radiation. [See section on RADIOGRAPHY.] Clinicians are concerned about using radiation that will, of course, strike the ovary. Seppanen's and Werner's teams advocate 'modern 100 mm. fluorography,' a low dose of X-rays and photographs which can be studied later (12,16). A new alternative is to use ultrasound — the Hyskon salpingogram — with the high-molecular-weight dextran Hyskon (7,16). See Section II for possible risks to progeny.

6) Pelvic Inflammatory Disease (PID). In Bateman's and Rice's recent studies three patients developed PID [Bateman: 1 out of 533 patients; Rice: 2 of 231] (2,12). Rice's patients were seriously ill. One had to have a total hysterectomy and salpingoophorectomy, and the other suffered extensive adhesions and occluded tubes that had been normal on the HSG. Each of these had had a previous bout with PID, and had not been given prophylactic antibiotics, which some other patients with PID had received (12). Thus, for Rice's second case, a subfertile woman became infertile through an infertility diagnostic procedure. However, it is clear that PID occurs very infrequently, at least in the clinics that submit articles to professional journals.

7) Adhesions. Bellina and Wilson claim that the dye itself can cause adhesions after leaving the tubes, and that, after a third HSG, a woman has a 25% chance of developing adhesions -- depending on her physiology and previous medical history (3).

8) Miscellaneous Side Effects. Patients who are tense or who always have severe menstrual cramps may get a vasovagal reaction, tubal spasms, false tubal blockage, or uterine cramps (14). Therefore Sheikh always gives atropine or Robinal, and, for apprehensive patients, diazepam or Motrin (13).

In sum, then, HSG is another diagnostic procedure that may bring about what it purports to cure.

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RISKS OF HYSTEROSCOPY

SUMMARY

Hysteroscopy for intrauterine visualization and surgery introduces the risks of hemorrhage, uterine perforation, plus the usual risks of surgery and those of laparoscopy (if this is done concomitantly). Risks unique to hysteroscopy are those associated with the distention media (CO2 or the dextran Hyskon) inserted under pressure -- for example, embolism as a hazard of CO2 use.

INTRODUCTION

Hysteroscopy is advocated by some as the best way of revealing defects inside the uterus and correcting many of them. The hysteroscope is a thin optical tube (xenon optics) that is passed through the cervix and into the uterus. First the uterus must be expanded with carbon dioxide or with a high molecular weight dextran, such as Hyskon. The operating channel for instruments in the hysteroscope permits surgery, such as removal of septa, barriers to the fallopian tubes, polyps and adhesions (1). Endometrial biopsy and sterilization may also be done with a hysteroscope.

General endotracheal anesthesia is commonly used (1,2), although some consider hysteroscopy an office procedure. For better visualization some teams do laparoscopy concurrently (2). Sometimes a balloon is inserted in the uterus afterwards for a day or two to keep uterine walls apart or to control bleeding.

ADVANTAGES

Advocates claim that hysteroscopy has several advantages over abdominal surgery (laparotomy) to correct uterine defects: "lower... morbidity, outpatient versus inpatient surgery, shortened recovery time until conception is advisable and obviation of mandatory cesarean delivery"(2).

RISKS

First, the usual risks of surgery: anesthesia accidents or allergies, blood vessel puncture and hemorrhage, nerve incision, accidental injury, etc. (See section on SURGERY.) Because laparoscopy is often used concomitantly, those risks are present. (See section on LAPAROSCOPY.)

Distention media put in under pressure also present hazards. Both media in common use may reflux through the cervix, compromising the efficacy of the procedure. Such reflux requires the use of grasping instruments on the cervix (4), which is potentially damaging to the cervix and painful if general anesthesia is not used. With CO2 distention the gas could enter a blood vessel leading to embolism (1). Corson and Batzer inject Pitressin to constrict blood vessels to prevent both hemorrhage and embolism (2). The dextran Hyskon used for distention may crystallize inside instruments (2) or cause an allergic reaction (1).

Another risk is bleeding, either during the procedure -- when it may block vision and make repeat hysteroscopy necessary (3) — or later after the patient has left medical surveillance, perhaps after Pitressin is no longer effective (2). And finally, there may be uterine perforation (5); Corson and Batzer reported diffusion of Hyskon through a thin cesarean scar as having the potential to perforate (2).

In sum, a procedure that ought to make pregnancy possible in women whose uteruses have structural defects carries with it significant risks of increasing infertility (6).

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RISKS OF LAPAROSCOPY

SUMMARY.

Risks of laparosocopy as used in IVF and GIFT on healthy women appear to have worried clinicians because many of them have (partially or completely) stopped using this procedure. Laparoscopy for chromotubation is part of the usual infertility workup. Morbidity after laparoscopy includes: shoulder pain, anesthesia after-effects, and blue urine after chromotubation. Potential complications include CO2 outside the peritoneal cavity, and, of course, those of all surgery: infection, arterial or venous hemorrhage, perforation of an organ, loss of an instrument in the body, — as well as cardiac or respiratory arrest, either of which could be fatal.

INTRODUCTION.

The laparoscope (or peritoneoscope or coeloscope) is an optical tube inserted into the abdomen for 1) diagnostic observation and testing of the pelvic organs (1); 2) guidance of oocyte retrieval for IVF or GIFT; and 3) and certain kinds of pelvic surgery. The first two purposes will be discussed here; the third, under 'pelvic surgery.' Laparoscopy usually requires pneumoperitoneum — the filling of the abdomen with CO2, Argon, or air to a positive pressure — to separate the abdominal wall from the internal organs. The head and shoulders are tilted down so that the intestines will slide away from the uterus (1) and to keep the CO2 away from the diaphragm (2). Local anesthesia is usually used for chromotubation; general, for oocyte retrieval. A tiny incision is made, usually through the navel.

Risks will be discussed in five categories: 1) the pneumoperitoneum; 2) anaesthesia; 3) chromotubation; 4) ovum pickup; and 5) risks of surgery. That many clinicians consider laparoscopy to be hazardous is shown when they write that they use another method because laparoscopy is 'undesirable' (16), has 'morbidity' (15) or has 'side effects' (4).

In interviews ten patients who had experienced both laparoscopy and ultrasonically directed oocyte retrieval unanimously preferred the ultrasound method and reported longer recovery times and greater pain and discomfort after laparoscopy (14).

1) PNEUMOPERITONEUM. Skilled personnel are required for CO2 insufflation. A common complication is that CO2 is not completely removed; it then irritates the peritoneal lining, and causes shoulder pain referred via phrenic nerve innervation of the diaphragm (2). Some patients consider this pain the most disagreeable part of IVF (8,9).

More serious are the possibilities of misplacement of the CO2 so that it enters some body part other than the peritoneal cavity, and acidosis which could induce cardiac arrest (2).

2) The risks from ANESTHESIA are the usual ones from anesthesia, such as vomiting, allergic reactions, respiratory arrest. An IVF patient in Stanford experienced a respiratory arrest which was promptly treated (2), but another in Sao Paulo Brazil died after being in a coma for five days (5). The latter was particularly dramatic because it occured on TV while the IVF team in Sao Paulo was televizing a 'course' in IVF taught by visiting international experts.

Anesthetic agents have been detected in follicular fluid (3); several studies show that oocytes collected later in the laparoscopic procedure are less likely to be fertilized, to develop, or to implant (6,11). Some have reported that the stress hormone response — always present in IVF -- is augmented under general anesthesia, affecting the luteal phase, leading to poorer implantation rates (12). When patients are asked, they always rank anesthesia high as a source of stress: for example, 42% of 50 IVF patients recently surveyed at Yale responded that anesthesia was the most stressful part of the procedure (13). If anesthetics do indeed have one or both of these effects (compromised fertilization and stress hormone augmentation), then use of anesthetics may contribute to infertility.

3) CHROMOTUBATION is the injection of methylene blue dye through the cervix so that tubal patency can be demonstrated. The dye is considered harmless; sometimes blue urine results. Patients do report pain. Could this dye cause or exacerbate pelvic inflammatory disease?

4) OOCYTE RETRIEVAL. Certainly some damage is done to the ovary; some believe that mechanical destruction to the follicles prevents them from forming good corpora lutea, causing luteal phase defect. [See section on Clomiphene under FERTILITY DRUGS.] And mechanical damage might trigger premature ovarian failure.

5) SURGERY. Errors in laparoscopy might occur during egg retreval: arterial or venous hemorrhage, organ perforation, or loss of part of the puncturing trocar, as happened in Bombay India (7).

Adhesions and infection are always risks in abdominal surgery (1). One IVF patient in New Zealand with a history of pelvic inflammatory disease experienced a severe resurgence after her IVF treatment (10).

In sum, then, laparoscopy is another technology with great possibilities, but also with the risk that its use may undo whatever good it does. What is unusual here is that many patients and practitioners have ackowledged problems (14,16).

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RISKS OF RADIOGRAPHY

SUMMARY.

Radiography in infertility diagnosis is limited, for all practical purposes, to hysterosalpingography. Risks to the patient are death of oocytes or embryos, or destruction of ovarian tissue, and oncogensis. Potentially serious risks to progeny are considered in Section II.

INTRODUCTION.

Since the inspired work of Alice Stewart in 1956 it is common knowledge that X-rays are dangerous and can cause cancer (4). Since Hiroshima, we know that radiation can kill, make people sick, and cause genetic damage. Thus only in emergencies are X-rays used in the pelvic area of a pregnant or potentially pregnant woman. About the only use in infertility diagnosis is hysterosalpingography (HSG). [See that section.]

Dangers from X-rays can be classified into 4 categories: 1) cytotoxicity (death of cells because of high dosages or cell susceptibility) 2) oncogenic (causing cancer); 3) developmental (causing a teratogenic effect); and 4) genetic (causing changes in DNA, either chromosomal aberrations or gene mutations). Possibly many or all oncogenic effects are the result of chromosomal aberrations or of activation of oncogenes. Therefore, category 4) might be the reason for 2), and might be divided into somatic effects on DNA (affecting the irradiated organism itself, probably through cancer) and germ cell alterations (affecting the progeny of the organism). Categories 3 and 4, plus oncogenesis in progeny, will be discussed in Section II (1,2,3,6).

1) CELL DEATH. At the preimplantation stage radiation injury usually causes embryonic death (3). Women may not know they are pregnant when an embryo is at this stage. Even though an HSG is usually done just before

ovulation, there could have been an early ovulation and a fertilized egg could get exposed and killed.

It is also possible that radiation of the ovary during HSG could damage ovarian follicle cells and immature oocytes so that the ovary might lose its ability to function. I have seen no data or speculations about this.

2) CANCER. Radiogenic cancers have very long latent periods, as seen in Table 1 (5). Thus we may not know for 20 or more years whether women who have had HSG are more likely to get cancer. Induction of leukemia in embryos and oocytes is considered in Section II (3,6).

TABLE I.

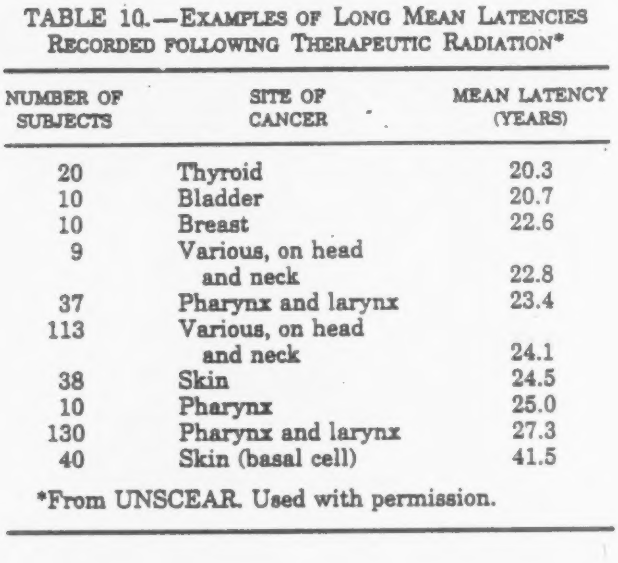

TABLE 10.—EXAMPLES OF LONG MEAN LATENCIES RECORDED FOLLOWING THERAPEUTIC RADIATION*

NUMBER OF SUBJECTS	SITE OF CANCER	MEAN LATENCY (YEARS)
20	Thyroid	20.3
10	Bladder	20.7
10	Breast	22.6
9	Various, on head and neck	22.8
37	Pharynx and larynx	23.4
113	Various, on head and neck	24.1
38	Skin	24.5
10	Pharynx	25.0
130	Pharynx and larynx	27.3
40	Skin (basal cell)	41.5

*From UNSCEAR. Used with permission.

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), "Report of the United Nations Committee on the Effects of Atomic Radiation: Sources and Effects of Ionizing Radiation," (New York: United Nations, 1977) p. 362. [reference #5; also in #6]

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RISKS OF DRUGS USED IN INFERTILITY TREATMENT

SUMMARY.

Hormones and hormone agonists used in therapy of infertility may induce luteal phase defect, hydatidiform mole, ovarian hypertrophy, premature aging of the ovary, ectopic pregnancy, and multiple gestation. Bromocriptine may have immediate side effects of nausea, vomiting, nasal stuffiness, and dizziness, and later, hydatidiform mole, mental disturbances, skin numbness, and even myocardial infarction; perhaps it makes women more susceptible to ovarian cancer after hyperstimulation. Any repeated therapy could be followed by menstrual irregularities or amenorrhea, ovarian failure, or ovarian cysts with ascites. Ovarian cancer is a long-term possibility. The effectiveness of progesterone and human chorionic gonadotropin in luteal phase support has not been demonstrated; their safety in women has not been studied. Repeated drug injection also risks allergic reactions and myocytis.

INTRODUCTION.

I classify drugs used for infertility treatment in seven categories: 1) clomiphene, used to help the pituitary produce gonadotrophic hormones; 2) bromocriptine, used when the pituitary overproduces prolactin, causing amenorrhea and infertility; 3) gonadotrophin releasing hormone (GnRH) or agonists to stimulate the hypothalamus; 4) gonadotrophins to stimulate the ovary directly; 5) human chorionic gonadotrophin (hCG) (which mimics luteinizing hormone (LH) surge and induces ovulation), injected about 36 hours before ovum pick-up; 6) corticosteroids to suppress adrenal androgen production; and 7) luteal phase support drugs, i.e., progesterones and hCG.

Since GnRH is not approved for use in the United States, category #3 will not be discussed, but I shall add a section #8 to discuss general hazards of repeated drug administration.

HAZARDS.

1) CLOMIPHENE. Clomiphene citrate (CC) is a triphenylethylene derivative which seems to have both estrogenic and antiestrogenic actvities.

One risk is that it may cause luteal phase deficiency (LPD), which can be defined as inadequate production of progesterone by the corpus luteum and/or inadequate response of the endometrium (12,38,45). LPD may lead to failure of implantation or early pregnancy loss. However, there are few adequately controlled studies, and failure to become pregnant can often be attributed to other factors in infertile patients. Yet CC may be able to induce LPD in normal women (38), thus potentially making fertile women subfertile.

A second concern is that vitamin B12 deficiency may be induced when CC is used in women who breviously were amenorrheic or oligomenorrheic (46). This apparently is not routinely checked after women have been on CC therapy.

A third concern is whether CC can induce birth defects if inadvertently it is given to pregnant women or if it remains in an active form in the body during the first few weeks of pregnancy. See discussion in Section II.

A fourth concern is hydatidiform mole -- an entity with an aberrant grape-like placenta -- which is more common after CC than in the general population (20). A mole is formed when two male pronuclei initiate development in an oocyte. One hypothesis is that CC stimulates the enlargment of some follicles whose oocytes' nuclei are not ready to complete meiosis I. Hydatidiform mole may be life-threatening if not removed promptly.

A fifth problem is ovarian hypertrophy. Ovarian hypertrophy is, in point of fact, the aim of CC therapy. The problem is whether it gets out of control during the therapy, or, much more serious, after the patient is no longer under regular medical monitoring, leading to cysts, then ascites or hemoperitoneum. Women who are taking CC for ovulation induction without IVF may be more at risk for cysts and ascites, for many practitioners believe that the puncturing of follicles during IVF egg retrieval is itself protection against hypertrophy (4,11). Among IVF candidates, Diamond et al believe that anovulatory women may be at lower risk of cysts (11). There are, however, reports of large ovarian cysts in current and ex-IVF patients (4,9) and of ovarian cancer (1,2,7,8); some consider these patients to be at risk of ovarian cancer over the next 10 or more years.

A sixth risk, for women who have many cycles of stimulation and egg retrieval, is premature aging of the ovary, or ovarian hypofunction. (This might be partly due to mechanical injury from numerous punctures, and not primarily to CC.) Foote found from personal experience and in the literature on hyperstimulation in cattle that after three or four cycles of stimulation most cows no longer superovulate reliably (13). Investigators who report on success rates with repeat IVF attempts on the same women have not mentioned this phenomenon. I have not seen any tables with numbers of eggs recovered in successive attempts. Most clinics do report a decreasing success rate chronologically per attempt, but not as much decline as one would expect if premature aging occurred. Indeed women have been reported to become pregnant after more than eight attempts.

However, this sixth risk is a particularly serious one for fertile women because it threatens loss of their fertility. At risk are fertile women who undergo ovulation induction before AID, for idiopathic infertility, for their husband's low sperm count, for donating eggs to a woman without ovaries, or for embryo lavage.

A seventh risk is future menstrual cycle irregularity, both volume of flow and periodicity (4), which could also render previously fertile women infertile. To the best of my knowledge, the Belaisch-Allert study (4) (which compares women with pure FSH stimulation versus those with CC-hMG stimulation) is the only one that has attempted to assess menstrual regularity in former IVF patients.

An eighth risk -- ectopic pregnancy — also may cause or exacerbate infertility. Clinics the world around report higher ectopic pregnancy rates; some workers believe that CC makes ectopic pregnancies more likely (22,25,26,28); others, simply, if more eggs, then statistically more ectopic pregnancies (10).

The eighth risk is one caused by any superovulation method: multiple gestation (38). Twin, triplet and quadruplet pregnancies have higher maternal morbidity and mortality.

2) BROMOCRIPTINE. Bromocriptine is an ergot derivate that has the almost miraculous ability to let women who have hyperprolactinemia become pregnant. In this defect, the pituitary produces too much prolactin (sometimes from a microlactinoma or a macrolactinoma) so that the patient's menstrual periods and ovulation cease and she has galactorrhea. Menstrual cycling usually resumes under bromocriptine treatment. (It is also used to suppress lactation and to relieve the symptoms of Parkinson's disease (44).)

Short term side effects. Those who start bromocriptine therapy almost invariably experience nausea and vomiting (16,27a,29a); they may have nasal stuffiness (27a,29a), headache (27a), digital vasospasm, and dizziness (orthostatic hypotension) (16,29a,36). To minimize these effects, advice is to start with low dosages and work up gradually, taking one dose at bedtime, and other doses always with meals (16,36). Some patients cannot tolerate the full infertility dosage, usually 2.5 mg of Parlodel (Sandoz' brand) twice daily (29a). (Much higher dosages are given to Parkinson disease patients.)

Longer term risks. Weil's recent literature review concludes:

> ...there is no indication that long-term bromocriptine treatment has harmful effects on hepatic, renal, haematologic or cardiac function. The various side-effects registered, most of them relatively benign, were shown in virtually all patients to be reversible... Bromocriptine was introduced on the market in 1973;...millions of patients have been treated with the drug... all the possible adverse effects of bromocriptine ought by now to have been identified... so that the discovery of a hitherto unknown severe though rare late adverse effect of bromocriptine is most unlikely (44).

Weil, however, is employed by Sandoz Limited. Other reports are not so sanguine. Psychological disturbances have been reported even at the low dosages used to treat hyperprolactinemia. For example, schizophrenic syndrome (41) and mania (43) in patients with no previous history of mental illness, and exacerbated mania in another (18). Related problems include depression, skin tingling, and numbness (27).

One fatality is clearly linked to bromocriptine at a low dosage. Iffy et al recently reported that two patients who received bromocriptine to suppress lactation had acute myocardial infarctions 10 days and 5 days, respectively, postpartum. The first survived after suffering a left ventricular aneurysm and the other died from an occluded branch of the left coronary artery (17). Iffy proposes that, although bromocriptine is usually a powerful vasodilator, it may sometimes display vasoconstrictor effects like some other ergot derivatives.

A patient receiving both CC and bromocriptine for a year developed bilateran ovarian carcinoma with metastases in the omentum in a cycle stimulated with CC, hMG and bromocriptine (7). Another patient with a past history of bromocriptine therapy also developed bilateral carcinoma in her third IVF attempt (8). Are bromocriptine and CC synergistic?

Also, hydatidiform mole occurs three times more often in pregnancies induced by bromocriptine: 0.2%, compared to 0.07% in control populations (16,29a).

4) GONADOTROPHINS. The most common gonadotrophin used in IVF ovulation induction protocols is Pergonal, which is Serono's brand of human menopausal gonadotrophin (hMG). Obtained from the urine of postmenopausal women, one dose contains 75 I.U. follicle stimulating hormone (FSH) activity and 75 I.U. luteinizing hormone (LH) activity. Some clinics have used 'pure' FSH, which actually has about 10% LH with it, but this more expensive preparation does not give consistently better results (3). A great many clinics use both CC and hMG in their protocols.

Because so many clinics use both, because protocols are constantly changing, because some clinics 'individualize' stimulation regimes, it is almost impossible to separate effects of hMG from those of CC. Thus, most risks attributed above to CC have also been reported from hMG: luteal phase defect, ovarian hypertrophy, premature aging of the ovary, ectopic pregnancy, and multiple gestation (38). Nowhere have I seen a discussion of whether menstrual cycles return to normality after treatment. Recently the first cases of hydatidiform mole after hMG induction have been reported (32,33,49).

In its package insert for Pergonal, the manufacturer Serono lists as 'adverse reactions': ovarian enlargement, hyperstimulation syndrome, hemoperitoneum, arterial thromoembolism, and sensitivity (39). One fatality has occured from thromboembolism (30). Serono reports that three patients had fevers after Pergonal shots, which might have been allergic reactions (39).

The concern about unintentional induction of infertility, described above under CC, applies here also.

5) HUMAN CHORIONIC GONADOTROPHIN (hCG). Some clinics try to identify the LH surge by analyzing blood or urine samples at frequent intervals and then scheduling ovum pick-up shortly after the surge. However, the vast majority induce ovulation by injecting hCG when the largest follicles reach a certain size (depending on the clinic), and then schedule ovum pick-up about 36 hours later. Because hCG for ovulation induction always follows CC or hMG (or both), its effects cannot be separated. (Indeed, FSH, LH, and hCG have very similar structures: they are two-unit polypeptides and have identical alpha subunits (40).)

To the best of my knowledge, there are no reports attributing any risks or side effects to the single hCG injection. (For longer term use, see 7b) below.) Serono's package insert states that in women hCG should be used in conjunction with hMG and gives under 'warnings' the first four adverse reactions to Pergonal (39,40). Additional adverse reactions listed probably refer to the use of hCG in males: headache, irritability, restlessness, depression, fatigue, edema, and gynecomastia (40).

6) CORTOCOSTEROIDS. The theory is that, since the stress of an IVF treatment may increase the adrenal output of androgens, suppression of the adrenal gland may improve ovarian response to stimulation. Dexamethasone and

pregnisolone have been used for this purpose. Kemeter obtained more oocytes and a higher pregnancy rate, compared to the controls, in a group treated with prednisolone (21). The general risks of tampering with the adrenal gland will not be discussed here; the risk of subjecting progeny to 'light for dates' reduction of intrauterine growth, should prednisolone be continued inadvertently during pregnancy, will be considered in Section II (34).

7) LUTEAL PHASE SUPPORT. Many practitioners are concerned about the low rate of implantation and clinical pregnancy after IVF and ET and have attributed this problem to luteal phase defect (12,45). The endometrium may not be in the right stage for implantation (from the fertility drug regime?) or the punctured or hormone stimulated follicle may not be able to form a properly functioning corpus luteum (38). In 1986 the global 'thing to do' experimentally was to run 'trials' comparing different drugs for luteal phase support (5,15,23,24,29,35,42,48). "Manipulation of the follicular phase... now is the rule in IVF programs..." (15).

Amond the drugs tried to 'cure' this defect are: progesterone (P) (because it is necessary for implantation and because normal corpora lutea produce large quantities); hCG (because this stimulates the corpus luteum to produce P).

7a) PROGESTERONE. P injections to sustain pregnancies in 'at risk' women have been given since the 1950s in some places (19,20). Natural progesterone and its derivatives substituted only in the alpha position on carbon 17 are metabolized quickly in the body and are inactivated if taken orally (6,19). No harmful effects on women have been reported from these. However, as far as I know, no one has assessed whether menstrual difficulties occur after pregnancies 'assisted' in this way.

Slower metabolizing derivatives of progesterone (pregnane derivatives) were used in early oral contraceptives and are no longer used because of their occasional serious side effects (6). Also these derivatives seem to decrease normal corpus luteum activity (12).

The 17-nor derivatives of testosterone, also considered progestogens, are not used for LPD because they masculinize female fetuses (19). This effect is discussed further in Section II.

7b) HUMAN CHORIONIC GONADOTROPIN. Apparently long-term use of hCG has not as yet been approved in the United States because the package insert does not mention its use in early pregnancy. One would expect some of the side effects listed in sections 4 and 5 above.

Reports that hCG is as miraculous at saving pregnancies as DES was purported to be, have come from England and The Netherlands, where some patients demand it. There it is extracted from urine donated by pregnant women. We should consider the fact that pregnant mare serum gonadotropin (PMSG) has been repeatedly demonstrated to be correlated with laboratory mammal embryo fragmentation, chromosomal abnormality, and embryo death (37).

7c) Are these effective? A moot question. The Johns Hopkins clinicians believe that P is very effective in high risk pregnancies (19,20). However, the several recent studies of luteal phase support in IVF programs published or reported at meetings give very equivocal results. Sometimes one treated group or control group has a higher percent of pregnancies than another, but results are rarely statistically significant (6,23,24,29,35,48). Indeed the team at Goteborg Sweden believes that exogenous hormones during early pregnancy may be more harmful than helpful (15).

8) GENERAL HAZARDS of repeated drug administration. The most obvious

hazard in this category is an allergic reaction, either to the active principle in a preparation or to the adjuvant. One IVF candidate died of asthma in New Zealand shortly before laparoscopy, after her hCG injection (14a). Serono reports cases of sensitivity to Pergonal (39). Why is 'nasal stuffiness' a common side effect of bromocriptine?

One could argue that there is always a risk of allergy in any medical drug treatment, but that this risk is taken if that particular drug is necessary to be cure a disease. What risks are worth taking to alleviate the symptoms of infertility? One would hope that infertility patients are questioned about their and their relatives' allergies, and that each program has an allergist on call, and for consultation afterwards.

A second general hazard, not life-threatening, but a source of morbidity is myocytis. I have met many thin and haggard infertile women. When so many intramuscular shots must be taken for follicle stimulation and later, for luteal phase support, one's muscles get quite sore. The site of injection of hCG may be particularly painful (40). Patients' personal accounts of their IVF experiences are most dramatic when describing this pain (31,47).

RECOMMENDATIONS.

See Section III.

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RISKS OF ARTIFICIAL INSEMINATION IN INFERTILITY TREATMENT

SUMMARY.

The genetic risk in artificial insemination is that abnormal genes or chromosome rearrangements will be transmitted to the resulting child. When the same donors are used repeatedly, unaware incest is a risk. Semen may carry pathogens that can cause mild to severe genital tract infections or severe systematic viral infections in sperm recipients. With such pathogens complications of pregnancy may include abortion, placental infections, premature delivery, and stillbirth. Intrauterine insemination risks uterine cramping and peritoneal infections. Other risks in AI include mental stress, allergies, and hydatidiform mole. Acknowledged even by enthusiasts, the serious risk of incurable and fatal AIDS has led to almost universal freezing of donor sperm for some months while donors have a series of tests for AIDS.

INTRODUCTION.

In infertility treatment, the palliative use of artificial insemination/donor (AID) or its variants artificial insemination/husband (AIH) and intrauterine insemination (IUI) (which may be either AID or AIH) may involve five or more parties: the sperm donor, the sperm recipient, the resulting child, the husband of the sperm recipient, and -- in cases of 'surrogacy' -- the social mother of the resulting child. (In the curious reversal of meaning instigated by Noel Keane, the person who raises the child as surrogate for the biological mother is not the 'surrogate.') Here I shall consider the hazards only to the sperm recipient and the resulting child.

I classify risks in six categories: 1)legal; 2) psychological/emotional; 3) genetic; 4) infectious; 5) from intrauterine insemination; and 6) miscellaneous. The first two will not be discussed here, even though, in my opinion, the hazards are far more serious in these two categories, especially because these can affect essentially all children resulting from AID. Legal matters include questions of adoption by the social father, of illegitimacy, of child support, of right of inheritance, of perjury (falsifying birth certificates)(4). Psychological/emotional hazards include falsehoods within a family (4,13,33), genealogical bewilderment (34), and concerns of children that their biological father cared more for money than for them (33).

GENETIC RISKS.

Genetic risk is -- simply -- the chance of producing a defective child. Either genes or chromosomes provided by the donor, when combined with those of the recipient, produce such a progeny. Or, two AID children, or one AID and one non-AID child, who do not know they have the same father, marry and produce such a child. (Unfortunately, I must ignore the nuances in the meaning of 'defective' in this discussion, although here semantics is vitally important.) The risks to the couple include lifelong physical care of a handicapped individual, vicarious suffering, and battles with social services. There is also an increased likelihood that a social father will refuse to provide financial and/or emotional support to a handicapped child not his own.

Curie-Cohen et al's landmark survey of 379 American physicians who had orchestrated some 3600 AID births in 1977 found inadequate screening of sperm donors, a lack of concern for the multiple use of donors, and inadequate record-keeping (12). Procedures were mildly positively eugenic in that medical students were the usual donors and "presumably... above average in intelligence and health" (14).

Although in the past AID practitioners have had little or no training in genetics, there is now considerable interest in involving geneticists in AID programs and with sperm banks (15,17,37,45). The network of sperm banks (CECOS) in France probably leads the world in this work. In one French study, 676 potential sperm donors were karyotyped and interviewed by a geneticist (37). Cytogenetic findings — usually minor chromosome rearrangements — excluded 2.6% of the potential donors; family genetic history excluded 3.4%. Some were accepted conditionally: their semen would be used only with recipients who did not have certain conditions in their family history. Selva and co-workers emphasize the difficulty of making exclusion decisions and the necessity of getting genetic information from the sperm recipient, too (15, 37). Their policy is clearly to avoid gross defects and not to do any positive selection. However, a type of screening goes on anyway in that CECOS attempts to match eye, hair, and skin color (26a).

The new ethical guidelines of the American Fertility Society provide for some genetic screening (2) and recommend that one donor not be used for more than 10 offspring (4,30) to help to avoid incest in the future (21). They also recommend that confidential and complete records be kept, and that nonidentifying information be released when important (4). However, these guidelines make no comment about the practice of sperm-mixing -- which could lead to untraceable paternity, even if records were kept (6a). The guidelines do not acknowledge that sperm-mixing has been practiced, nor take a stance. Indeed, they actually approve of sperm-mixing in the context of IVF (6): when the husband's sperm does not fertilize the eggs, "..the use of donor semen as a backup system for IVF is then justifiable."(6) **See also (44).**

INFECTIONS.

A variety of viral, mycoplasmal, and bacterial infections may be transmitted in semen. Table 1 lists these diseases and whether their transmission in AI has been reported (20). "These sexually transmitted pathogens are associated with a wide variety of disease states in women, ranging from mild infection of the vagina to severe invasive bacterial infections of the upper genital tract that may cause tubal scarring, and severe systemic viral infections, now including AIDS." (20) The actual rate at which these infections has occured is shown in Table 2 (27). Diseases transmitted include infection by the mycoplasma Ureaplasma urealyticum (8), gonorrhea (16,39,43) and AIDS. What is probably the first fatality from AIDS transmitted by semen donor was reported from New South Wales in 1986. Four women who had used the same donor had AIDS antibodies in their sera; three were still alive in early 1986 (29). Acknowledged even by enthusiasts, the serious risk of incurable and fatal AIDS has led to almost universal freezing of donor sperm for some months while donors have a series of tests for AIDS.

Some pathogens can complicate pregnancy; possible complications are listed in Table 3 (20).

INTRAUTERINE INSEMINATION.

Insemination directly in the uterus is used in cases of hostile cervical mucus and anti-sperm antibodies in mucus (1). Its success rate, however, is poor, and complications are likely (23,24,42). Apparently semen contains a great quantity of prostaglandins which may trigger uterine contractions. If sperm swim through cervical mucus, prostaglandins are left behind. Therefore IUI sperm must be properly washed (1,24,31).

Another problem with IUI is bleeding from inadvertently poking the endometrium (1). However, pelvic inflammatory disease has not been reported (41), even though Stone et al were able to recover organisms present in donor semen from the peritoneal cavity after IUI (42). And, if a woman has anti-sperm antibodies, their titer may increase after IUI because of the large concentration of sperm in the uterus (1).

MISCELLANEOUS.

Other complications have been reported for AI. 1) stress and mental distress, including post-partum depression (7,31). One stressful factor is the low success rate: Jackson and Richardson report that patients were inseminated 6.7 times on the average (23a). 2) There may be a higher chance of hydatidiform mole (32a). 3) If donor semen is mixed with the husband's semen, there may be agglutination if the husband's semen contains antisperm antibodies.

TABLE 1.

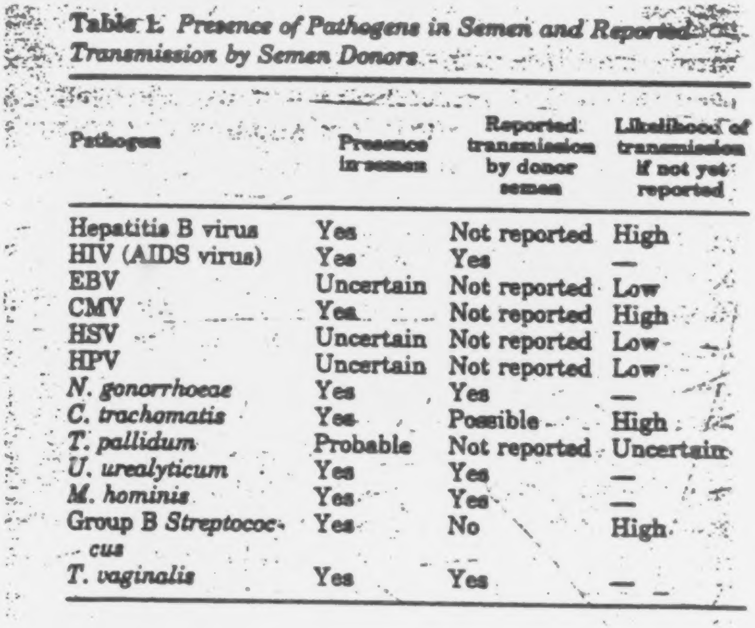

Table 1. *Presence of Pathogens in Semen and Reported Transmission by Semen Donors*

Pathogen	Presence in semen	Reported transmission by donor semen	Likelihood of transmission if not yet reported
Hepatitis B virus	Yes	Not reported	High
HIV (AIDS virus)	Yes	Yes	—
EBV	Uncertain	Not reported	Low
CMV	Yes	Not reported	High
HSV	Uncertain	Not reported	Low
HPV	Uncertain	Not reported	Low
N. gonorrhoeae	Yes	Yes	—
C. trachomatis	Yes	Possible	High
T. pallidum	Probable	Not reported	Uncertain
U. urealyticum	Yes	Yes	—
M. hominis	Yes	Yes	—
Group B *Streptococcus*	Yes	No	High
T. vaginalis	Yes	Yes	—

Greenblatt,R.M., Handsfield, H.H., Sayers,M.H., and Holmes, K.K., "Screening Therapeutic Insemination Donors for Sexually Transmitted Diseases: Overview and Recommendations," Fertility and Sterility 46:351-364, 1986. (page 359)

TABLE 2.

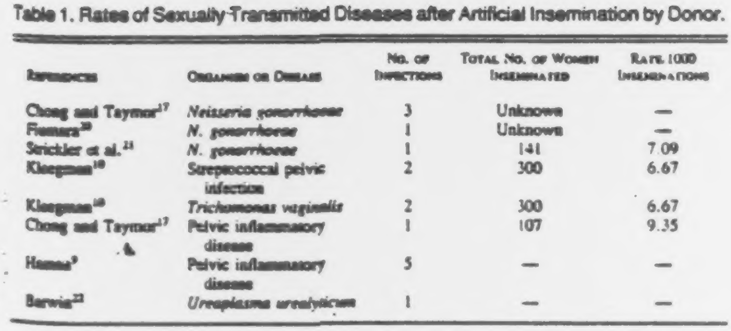

Table 1. Rates of Sexually Transmitted Diseases after Artificial Insemination by Donor.

References	Organism or Disease	No. of Infections	Total No. of Women Inseminated	Rate 1000 Inseminations
Chong and Taymor[17]	*Neisseria gonorrhoeae*	3	Unknown	—
Fiumara[20]	*N. gonorrhoeae*	1	Unknown	—
Strickler et al.[21]	*N. gonorrhoeae*	1	141	7.09
Kleegman[10]	Streptococcal pelvic infection	2	300	6.67
Kleegman[10]	*Trichomonas vaginalis*	2	300	6.67
Chong and Taymor[17]	Pelvic inflammatory disease	1	107	9.35
Hamns[9]	Pelvic inflammatory disease	5	—	—
Berwin[22]	*Ureaplasma urealyticum*	1	—	—

Mascola,L., and Guinan,M.E., "Screening to Reduce Transmission of Sexually Transmitted Diseases in Semen Used for Artificial Insemination," The New England Journal of Medicine 314(21):1354-1357, 1986. (page 1355)

In a response to criticism of this paper, Mascola and Guinan corrected the first reference from 'Chong and Taymor' to 'Hansen et al' (28).

Citations to the eight entries in this table may be found in the reference list starting on page 60, as entries 21b, 16, 43a, 26, 26, 10, 21a, and 8, respectively.

Table 2. *Reported Effects of Sexually Transmitted Pathogens on Pregnancy, Fetus, and Infant*

Pathogen	Reported effects on pregnancy[a,b]	Effect on fetus/infant[b]
Viruses		
Hepatitis B virus	None known	Perinatal transmission, chronic carriage, chronic hepatitis
Cytomegalovirus	? Prematurity, ? Spontaneous abortion	Congenital and perinatal infection, malformation
Herpes simplex virus	Prematurity, abortion, asymptomatic shedding	Congenital and perinatal herpes, encephalitis
HIV (AIDS virus)	Prematurity	Congenital and perinatal infection, AIDS, ARC
Human papillomavirus	Giant condylomata	Laryngeal papillomatosis, genital warts, ? latency
Epstein-Barr virus	None (?)	None (?)
Bacteria		
N. gonorrhoeae	Abortion, stillbirth amnionitis, endometritis PROM, IUGR	Neonatal conjunctivitis, sepsis
C. trachomatis	LBW, PROM, endometritis	Neonatal conjunctivitis, pneumonitis
T. pallidum	Abortion, stillbirth, prematurity	Congenital syphilis
U. urealyticum	Prematurity, LBW	? Pneumonitis
M. hominis	Postpartum fever, endometritis	Neonatal sepsis (rare)
Group B streptococcus	Prematurity, PROM, chorioamnionitis, postpartum endometritis	Neonatal sepsis and meningitis
Protozoa		
T. vaginalis	Vaginitis	Vaginitis

[a] Effects on pregnancy per se, in addition to usual effects of acute infection; see text for description. Reports based solely on anecdotal observations are not included.

[b] PROM, premature rupture of membranes; IUGR, intrauterine growth retardation; LBW, low birth weight; ARC, AIDS-related complex.

TABLE 3

Greenblatt,R.M., Handsfield, H.H., Sayers,M.H., and Holmes, K.K., "Screening Therapeutic Insemination Donors for Sexually Transmitted Diseases: Overview and Recommendations," Fertility and Sterility 46:351-364, 1986. (page 359)

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RISKS OF ULTRASONICALLY DIRECTED OOCYTE RETRIEVAL

SUMMARY.

Methods of ultrasonically directed oocyte recovery (transabdominal, periurethral, and transvaginal) may contaminate fluid surrounding retrieved oocytes, thus compromising fertilization and cleavage; the ultrasound itself may damage oocytes or future corpora lutea. Infertile women have suffered pain, short-term hematuria, and blood vessel puncture; more serious risks are pelvic infection, hemorrhage, and vaginitis. One survey reports only one fatality in several hundred attempts. Serious questions need to be asked about methods that encourage independent private practices away from hospital human subjects committees and into the 'marketplace.'

INTRODUCTION.

Concern about the trauma from laparoscopic ovum recovery has led many investigators over the past 4 years to attempt less traumatic ways of obtaining oocytes. Early on, some of these methods were called "non-surgical" because they avoided total anesthesia, especially the endotracheal intubation used with laparoscopy. Terminology in the medical literature now is often "Ultrasonically Guided," "Ultrasonically Directed" or "Sonographically Controlled," and "Ovum Pick-up," "Oocyte Recovery," "Oocyte Retrieval," "Follicle Aspiration," or "Follicle Puncture." I shall use 'UD' and 'OR.'

Three basic routes for OR are used (and combinations sometimes): 1) transabdominal (percutaneus)/transvesical; 2) perurethral; and 3) transvaginal. Patients may receive no anesthesia, local anesthesia around the site of needle puncture, light epidural anesthesia, sedation (often atropine, pethidine and/or diazepam), or, in a few clinics, total anesthesia. The hollow needle is guided to each ripe follicle by tracing its movements on the ultrasound screen and then the contents of each follicle is siphoned out. In 1983 and 84 the ultrasound transducers were placed on the abdomen. Then the vaginal transducer was invented and became commercially available in September 1985 (ref). Now this is almost exclusively used, regardless of the route of OR; however, sometimes both an abdominal and a vaginal transducer are used together (ref).

It is interesting that clinicians reporting their success rates after UDOR sometimes fail to mention the route they used! I have included no such reports in the references here. To guess from global medical fashion; in 1984 and 85, the transabdominal route was the favorite; in 86 and 87, the transvaginal.

Several investigators extol the virtues of these UD methods as great improvements over laparascopic retrieval (See references 4,15,16 on pages 32, 33 and discussion under "Risks of Laparoscopy.")

ROUTES AND POTENTIAL HAZARDS OF EACH.

1) Transabdominal (transvesical). This method was pioneered by Lenz of Copenhagen followed shortly by Wikland of Goteborg (8,5). The patient's bladder is filled with sterile saline or other isotonic solution. The needle passes through the abdominal wall, through the bladder wall and out the bladder wall directly into the ripe follicles. A separate puncture is made for each follicle (5,8). The one variant I have found is the transvesical/ transuterine in which, because the ovaries are behind the fundus of the uterus, the uterine wall must also be punctured. Since two successful pregnancies (to term) have been obtained after using this route, it apparently does not harm the endometrium and myometrium (9). However, the investigators do not give the number of patients on whom the technique failed.

Potential Hazards. a) To success of IVF. In the literature, when lower fertilization rates (than in oocytes obtained by laparoscopy) were encountered, speculations were that this was due to contamination of the culture medium with urine. Early on when fewer oocytes were obtained, this was attributed to inexperience with the technique (ref) or poor visualization on ultrasound. Change from abdominal transducers to vaginal ones is said to improve the latter. Also concern has been raised about fewer oocytes cleaving and poor success in implantation because of harm to the oocyte from the considerable focussed ultrasound necessary for egg retrieval using this method, or from "disordered luteal phase endocrinology," meaning, I believe, that a proper corpus luteum may not form after excessive ultrasound (15).

b) to total health of potential IVF mother. Complications reported are discomfort from the full bladder, pain (3) and short-lasting hematuria (9). However, mid-term and long-term sequelae have not been considered nor have (to my knowledge) plans been made to discover them. Such sequelae might include: a susceptibility to or recurrent hematuria; leakage of urine into the abdomen; earlier incontinence (earlier than usual in old age); adhesion of bladder to ovary; susceptibility to cystitis.

2) Perurethral. This route was pioneered by Parsons in London. Again, the bladder is filled with sterile saline. A hollow tube is inserted into the urethra. The needle for ovum pick-up is inserted through this tube and then it is moved into the urinary bladder. It punctures the bladder near each ripe follicle in each ovary.

Potential hazards. a) to success of IVF: The same speculations have been made as with the transabdominal method (refs).

b) to total health of potential IVF mother. Both discomfort from the full bladder and pain have been reported (ref). Stronger anesthesia has usually been used for this method. However, in one experiment in which women were asked to assess their pain subjectively, no differences between transvaginal and perurethral were reported (13?).

Hematuria and discomfort while urinating for a day or two are expected side effects. The one patient I interviewed had had hematuria and painful urination for only one day. The potential mid-term and long-term sequelae mentioned above also pertain here. I hypothesize, however, that these later sequelae will be more severe with perurethral OR, particularly cystitis, recurrent hematuria and borderline or early incontinence.

3) Transvaginal. Pioneered by Dellenbach and his team at Strasbourg, by 1987 this method of OR has become the most popular (2,3). The ovum recovery needle is inserted through the wall of the vagina, the posterolateral vaginal pouch first on one side, then the other. Some vaginal transducers have needle guides on them. Often the patient is given a paracervical block as local anesthesia.

3a) One variation of transvaginal OR is transvaginal/transvesical OR, used when the ovary is higher up, in which first the anterolateral vaginal pouch is punctured, then the urinary bladder, then each ripe follicle. Of 177 punctures in the Necker Hospital in Paris, 107 were simple transvaginal and 88 went also through the bladder.

Potential hazards. a) to success of IVF: as above. In addition there are worries that microorganisms from the vagina may contaminate oocyte cultures. Some workers disinfect the vagina with Betadine, but others who have had poor results in IVF or oocyte division after transvaginal OR, hypothesize that disinfectants may have deleterious effects on oocyte culture.

b) to total health: Reported mishaps and side effects include iliac vein punctures and severe vesicular or pelvic pain requiring 24 hour hospital admission. No hematuria has been reported for the transvaginal/ transvesical. Iliac vein punctures have no severe sequelae if the needle is withdrawn rapidly with no tearing. The team from Necker Hospital is very concerned to avoid puncture of the rectum or the intestine which could lead to pelvic infection. They avoid this by puncturing only those ovaries which are determined by ultrasound to be in contact with the vagina or the bladder, so that the needle does not pass through any unidentified space. They also believe that pelvic infection is avoided by disinfecting the vagina thoroughly.

In sum, then, short-term serious sequelae could include venupunture, pelvic infection, damage to intestine or rectum requiring surgical repair, reactions to one or more sedatives and local anesthetics. Mid-term and long-term sequelae have -- to my knowledge -- not been sought. These might include: vaginitis from disturbing the normal flora of the vagina; painful coitus; pelvic infections which might remain asymptomatic for months or years; chronic internal blood leakage from venupuncture.

GENERAL COMMENTS.

In a study of UDOR methods at 20 centers over two years only one fatality occurred. What mortality rate is acceptable? How can we be certain that there is not a cover-up of other deaths, or that they are attributed to other causes, which is easy to do if the death occurs after the procedure.

Enthusiastic users of UDOR cite various reasons for their enthusiasm. However, each reason demands careful scrutiny. 1) UDOR avoids the dangers of anesthesia: Anesthesia during laparoscopy has been shown to cause hyperprolactinemia which may cause luteal phase deficiency, making implantation more difficult (10). However, in practice many teams use considerable sedation and local anesthesia; some use general anesthesia, at least for their more anxious patients. Others expect stoic endurance of pain.

2) UDOR is cheaper. This means that patients need not pay for operating room and personnel, especially anesthesiologists. Even though one avoids the risks of endotracheal intubation, the absence of specialists may put patients at risk from less dangerous anesthetics and sedatives.

3) UDOR is an outpatient procedure. The patient need not stay overnight in a hospital, nor even enter its doors. However, even from UDOR complications may arise for which hospitalization is needed. The patient may be sent home from the office before sequelae are evident. But, the real sleeper in this 'benefit' of UDOR is that doctors are now removed under the scrutiny of hospital ethics committees. This means that physicians can try any variations at all that may happen to occur to them without justifying it to their peers; their methods of obtaining 'informed consent' are also not reviewed. Free enterprise, the 'market,' some say, will guarantee effective methods. Unfortunately, there is no way that patients can get verifiable statistics about any IVF program, private or public; indeed, desperation to get a baby often makes them willing to try anything. (However, participation in a university-based IVF program, with all its human-subject-review machinery in place, does not guarantee patient safety because of the publish-or-perish imperative that drives its staff to keep doing experiments for the sake of experimenting.)

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RISKS TO THE PROGENY

SUMMARY.

Although most surveys of progeny born after infertility treatments show either no significant difference in abnormalities compared to control populations or only slight increases, weaknesses in methodology may unintentionally fail to access the most negative data. And, as far as I know, no studies (except for those on DES, not considered herein) have sampled progeny at or above the age of puberty. The most commonly reported anomalies and problems are those associated with multiple gestations and preterm deliveries. Areas that need to be considered are: 1) from ultrasonography: possible cancer induction and teratogenic effects, particularly from the repeated monitoring during early pregnancy establishment; 2) from radiography (hysterosalpingography): progeny of women who had ever had an HSG, possible cancer, developmental or genetic birth defects....

CAVEATS.

Some arbitrary decisions were made in writing this section. First, although I consider that the risks of legal and psychological/emotional problems are far more serious to progeny than biological risks, those more serious risks will be mentioned only occasionally: this report will focus on the biological risks. Second, I have arbitrarily defined progeny as the live-born child. Thus, any factors that prevent a conceptus from implantation, growth, or development in the uterus have been considered in Section I. Each diagnostic procedure and treatment is considered in order.

CERVICAL MUCUS EVALUATION.

One problem that a progeny might face would be from being unwanted because of a false-negative evaluation.

ENDOMETRIAL BIOPSY.

One could speculate that if an endometrial biopsy were done to a pregnant uterus and the fetus survived, that a disturbance of the implantation site might cause a developmental defect. This is unlikely.

ULTRASONOGRAPHY

SUMMARY. Although there is no unequivocable proof, risks of cancer, teratogenesis, and growth retardation from the usual use of obstetric ultrasound seem low, possibly non-existent, although neurological effects have not been well studied. But studies of the sequelae of ultrasound irradiation of human oocytes and very early human embryos, where most exposure occurs in IVF, have not been done.

RISKS OF OBSTETRIC ULTRASOUND. See the subsection ULTRASONOGRAPHY in Section I for a discussion of what is meant by obstetric ultrasound and a summary of recent international and national group meetings and symposia.

Studies of children who were exposed to ultrasound (US) in utero have generally failed to demonstrate increased birth defects or effects on height and weight (14,15,18,31). However, recent case-control studies on possible cancer induction from antenatal US have given conflicting results. Kinnier-Wilson and Waterhouse found 4.3 times the expected incidence of cancer in children over 6 years (12,17); Cartwright et al found no increase (2,17).

However, because the two time periods when obstetric US is most often used coincide with the development of the cerebral hemispheres (16-18 weeks) and with the development of the cerebellum (32-34 weeks)(17), it seems most logical to look for effects of US on the central nervous system. Visual and hearing deficits have not been found (17,31). One report of increased dyslexia in children prenatally screened with US has raised much interest, but also criticisms that variables were not controlled (10,24,29,31). Although design of studies on cognition and other mental faculties that will pass both scientific and ethical scrutiny is extremely difficult (17), the central nervous system may well be the locale for adverse effects of US.

RISKS OF ULTRASOUND AS SPECIFICALLY USED IN INFERTILITY TREATMENTS. As described as #2 of "Pertinent Risks" in ULTRASONOGRAPHY under Section I, the early embryo may receive considerable US as the pregnancy is monitored in its early weeks to watch for ectopic pregnancies and to determine whether implantation has indeed occurred. This would be in the period of primitive streak formation, neural tube formation, and early organogenesis; one could postulate that US at this time would be teratogenic.

Animal work, however, has not produced any "confirmed reports of teratological effects of pulsed utrasound in the clinically relevant range." In small laboratory mammals US at high intensities and durations has indeed caused deleterious developmental effects, decreased fetal weight and malformations related to stage of gestation at exposure. Because of higher dosages used and interspecific differences, results with animal studies are essentially meaningless when transferred to humans.

There are currently relatively few progeny who were US-monitored at this early stage of development, although since 1983 essentially all IVF children fall in this category. Whether very early pregnancy monitoring with US is teratogenic is still an open question.

As described as #6 of "Pertinent Risks" in ULTRASONOGRAPHY under Section I, inactive oocytes in diplotene stage are irradiated with US during monitoring of follicle growth. This might lead to chromosome anomalies in a later attempt at IVF. Tabulations of birth defects in IVF children (21) have not, however, tallied children separately as ones whose ovum of origin might have been irradiated in the diplotene stage.

HYSTEROSALPINGOGRAPHY

Since a hysterosalpingogram requires X-rays, teratogenesis is possible should a fetus receive X-irradiation during early organogenesis if a patient were unknowingly pregnant when she came for a HSG. Because of the timing for the HSG, a woman might be about four weeks pregnant. As far as I know, there are no reports of followup of the few such progeny mentioned in the literature. Werner calculated the dose on 100 (nonpregnant) patients and determined that it was far below the 10 rad level for terminating a pregnancy, as determined by the Israel Ministry of Health (34). Also, a woman's oocytes in diplotene stage would get X-irradiation during each hysterosalpingogram. See RADIOGRAPHY below for further discussion.

HYSTEROSCOPY

Since it is unlikely that any fetus could survive hysteroscopic examination or surgery, developmental teratogenetic effects would be impossible.

LAPAROSCOPY

A few cases in the literature report laparoscopy in women who were unknowingly pregnant and then successfully carried that pregnancy to term. The infants were not defective in any way. The instruments and procedures of laparoscopy are not likely to have a teratogenic effect, but anesthesia might, especially during early organogensis. It would be very difficult to separate the effects of anesthesia from the effects of the prelaparoscopic fertility drugs given inadvertently to the pregnant woman.

RADIOGRAPHY

Practitioners are very cautious about using X-rays on pregnant or potentially pregnant women. Thus in an infertility workup, hysterosalpingography (HSG) is the only treatment when this radiation is likely. Experts who have calculated the radiation dosages currently used in HSG are certain that they are much too low for any of the below effects (20).

CANCER. Since the inspired work of Alice Stewart in 1956 it is common knowledge that X-rays during fetal development can trigger cancer, especially leukemia (30). Embryos at all stages are susceptible; some think that leukemia can even be induced in an oocyte (Whalen). As far as I know, no one has followed up the progeny of those few women who were pregnant when they had an HSG.

TERATOGENESIS. As shown by the data for mice and humans in Table 1, specific damage will be induced when an embryo or fetus is irradiated at a specific point in its development, when a given organ is developing (25,26, 34). This is called a nonstochastic risk because it is not random. During an HSG an embryo might be at 24 to 30 gestation days. Note in Table 1 the long periods of time when parts of the central nervous system are developing -- making the fetus very susceptible to gross and subtle neurologic anomalies.

MUTATIONS. Effects of X-rays on DNA are stochastic, i.e., random. A low level dose could happen to trigger a mutation. Since a women's oocytes are already in the diplotene stage before she is born, they are considered to be resistant to radiation damage, so a chance low dose mutation is highly unlikely. (Spermatogonia are far more susceptible.)

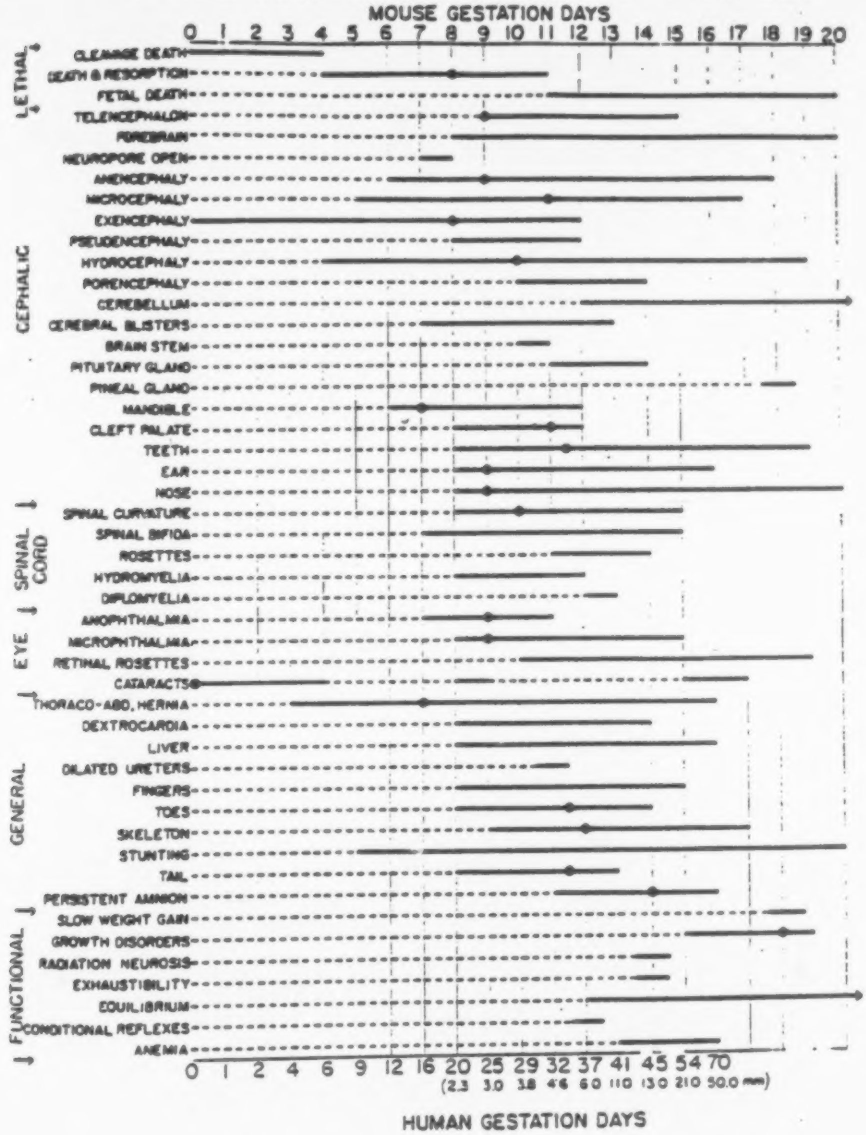
Any genetic effect of X-rays on oocytes during HSG would appear in offspring conceived after HSG. As far as I know, studies have not been done of all progeny of women who ever had HSG.

FERTILITY DRUG THERAPY.

CLOMID.

TABLE 1.

X-IRRADIATION-INDUCED CONGENITAL ANOMALIES



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AREAS WHERE ADDITIONAL RESEARCH IS NEEDED

PROSPECTUS.

This section suggests additional research for making infertility diagnosis and treatment more effective and less hazardous. In a few cases, studies for better education of patients and/or professionals are proposed.

First I discuss five general researches that are not tied to one specific diagnostic or treatment procedure, and then I discuss most of the areas of Sections I and II in order.

This Section has only a brief reference list. A few citations in the text indicate a previous page in this document, i.e., (p.n), or a reference on such a page, i.e., (#n,p.n).

AN ETHICAL SCIENTIFIC EXPERIMENT?

I shall also 'beg' the question of designing an experiment with human subjects that is both 'scientific' and also 'ethical.' Frankly, I think it is impossible. One of the most often cited dilemmas is how can you give one treatment (or a placebo) to one group of patients if you really believe that the other treatment is more effective. In infertility treatments, as discussed in Section I, practitioners may hold strong beliefs that one treatment is better than another, when each is minimally effective.

In the area of infertility, patient desperation adds another confounding factor. With infertility, assertive and healthy couples actively demand their right to treatment. Such demand — when coupled with surgeons' fascination with the new techniques plus the thrill of manipulation that had led them to become surgeons -- makes a synergism that is very difficult to resist.

Furthermore, for biological reasons a properly controlled experiment is difficult to design. Frequent reports in the literature tell of pregnancies obtained without any treatment, e.g., by women on waiting lists, those who merely had a diagnostic test, those who had decided to adopt. Also no two women are alike in physiology, or in previous history of injury and disease.

GENERAL RESEARCH.

1) First, we should take a hard look at exactly where problem-solving in infertility has been successful. Bellina says, "Science has been so successful that 90 pecent of all cases of infertility today can be accurately diagnosed, compared with only 40 percent ten years ago."(#3,p.24) Is this indeed true? People who have no vested interest in one or another procedure ought to design a study to determine (1) how accurate diagnosis actually is in the mid-1980s, and/or (2) what treatment methods have really cured or palliated infertility. Perhaps an epidemiologist who is part of an infertile couple would be an appropriate investigator.

2) Goals need to be properly defined in all units that deal with the infertile, and to be part of the training of new gynecologists. One must be able to draw the fine line between offering real help to the infertile and wanting to perform (or learn, in the case of gynecologists-in-training) some intriguing technique.

A corollary to this is the 'knowledge for the sake of knowledge' or 'science for the sake of science' position. Is knowledge (or science) a good in itself? The glib answer is, 'yes, of course, because ignorance is clearly an evil.' But the problem is more subtle. First, if one uses gaining of knowledge as a fundamental normative principle, then one may easily blind oneself to other considerations. Whatever the 'ethics' of physicians is, it includes the concept that doing experiments is a 'good' in itself. This is demonstrated by the 1984 statement of the American Fertility Society, "In view of the many research opportunities offered by programs of in vitro fertilization, it is urged that all programs be designed to take advantage of these opportunities." (#1,p.95) Women may be assigned to an experimental group simply in order to have IVF. Such assignment can be unethical for a variety of reasons. The only certain benefit is prestige to the clinician for being able to define him/herself as a researcher. Furthermore, the choice of experiment may depend on the global fashion at the moment. (See discussion, p. 44.) Indeed, doing something may be worse than doing nothing (#15, p.48).

A second problem with 'knowledge for the sake of knowledge' is that one may uncover knowledge that can lead to great evil. For example, knowledge of the structure of the atom has led to the creation of such lethal weapons that world diplomats have to put tremendous time, energy, and money into negotiating how to control this instead of into relieving human misery.

3) Prevention of infertility should have the highest priority; research should be done at both the biological and psychological levels.

a) Applied Research. Among many possibilities, three examples are the design and production of (i) educational programs, (ii) home testing kits for venereal diseases, and (iii) home methods for reestablishing monthly ovulation.

b) Cervical mucus evaluation should be taught standardly in sex education and in a teenager's first visit to a gynecologist.

c) Better statistics should be obtained to correlate infertility with: (a) occupation, (b) life style, and (c) environmental pollution.

d) Surgeons should work on developing methods of abdominal surgery that result in fewer adhesions. Some persons are adhesion-prone and others are not (#3,p.24). Studies should be done to learn how to identify beforehand adhesion-prone physiology in a patient.

4) Because many women work to establish a career before having a family, and because fertility decreases with age, this problem needs to be attacked

with a multi-faceted approach. Job-sharing and/or child-care at workplaces might encourage earalier child-bearing. However, since later age at reproduction is an excellent way of population control, methods of preserving fertility as discussed in 3) above should be researched and promulgated.

5) Finding the Unexpected. Fifteen years after diethylstilbestrol (DES) was used in the 1950s as an antiabortifacient the rare clear cell carcinoma of the vagina was discovered in daughters who survived those pregnancies. We continue to uncover a plethora of other reproductive tract abnormalities in DES daughters and sons. We are also finding increased breast cancer in the mothers (#2,p.95). It behooves us to be alert to the sequelae of infertility treatments of the 1980s. From about 1993 on, we should systematically record the complaints and conditions that women over 40 bring to gynecologists, and adolescent children from fertility-drug-treated mothers. What will be the 'clear cell cancer' of the 1990s?

SECTION I: RISKS TO THE COUPLE

CERVICAL MUCUS EVALUATION.

Of the methods discussed in Section I, I endorse only this without reservation. Sex education should include learning this evaluation; methods to restore proper and normal cycling mucus should be researched (#1,p.3).

ENDOMETRIAL BIOPSY.

Research is needed on better methods of evaluating the condition of the endometrium. Here again is the problem of designing a properly controlled experiment on a technique that is painful and potentially dangerous.

One question is whether serum progesterone determinations can do as good a job at evaluating luteal phase endometrium (#1,2,9,p.6); another is how to improve the record on false positives and false negatives, with the goal of avoiding repeat biopsies (#2,10,12,p.6); a third is how to fabricate sampling devices that are less painful and give less morbidity (#2,p.6).

ULTRASONOGRAPHY.

Most recommended additional research in this area concerns the effects of ultrasound on progeny and will be discussed under 'SECTION II.'

Does ultrasonic exposure of ovaries increase infertility? A larger study similar to Demoulin's (#11,p.16), using US-exposed and unexposed groups, should be designed for infertility treatments where US is really unnecessary, i.e., AID and fertility drug treatment with natural intercourse. Such a study would determine whether pregnancies were more likely with or without ovarian exposure to US; it would have to be extensive so that individual variation in physiology would not be a confounding factor.

Another possible approach to this question would be a retrospective study of fertilization success rates in a given clinic before ultrasound was used routinely, and then afterwards. (Unfortunately, a confounding factor here is the fact that, as experience is gained, fertilization rates improve.)

HYSTEROSALPINGOGRAPHY.

Necessary additional research about the effect of the radiation in hysterosalpingography will be discussed under 'RADIOGRAPHY' and 'SECTION II.' Here we consider the effects of the contrast media.

Sorely needed are multi-center studies of mid- and long-term effects of hystersalpingography. If patients with sequelae take their problems to internists, gynecologists may not be aware of them. Neutral parties ought to systematically investigate such possible sequelae as: cancer, embolism, intravasation, granuloma, pelvic inflammatory disease, adhesions.

1) A prospective study of short- and mid-term sequelae should be designed with current HSG participants. Names and addresses of three close friends or relatives, of same or younger age, should be obtained to facilitate

tracing patients in the future. Matched controls should be set up.

2) A follow-up (retrospective) study of women who had HSGs should be carried out. If patients from more than 20 years ago can be found, good information about the above-mentioned sequelae should be forthcoming. Matched controls are, of course, necessary.

3) Using existing IVF data banks, such as the National Perinatal Statistics Unit in Australia (#21,p.81), success rates in IVF should be compared: women with HSGs in their infertility workups versus those without.

4) Multi-center data should be collected on the rates of false-positives and false-negatives (re tubal patency) from HSG. What percent uncertainty can justify using a risky procedure?

HYSTEROSCOPY.

Possible sequelae such as embolism, hemorrhage, adhesions, uterine perforation, and infection need to be studied in prospective and retrospective studies, as for hysterosalpingography, pages 88-89, 1) and 2).

LAPAROSCOPY.

1) Chromotubation: Sequelae after chromotubation ought to be studied as for hysterosalpingography, pages 88-89, 1) and 2).

2) In centers that have chosen to continue to use laparoscopy in IVF/ET and GIFT, more systematic recording of patient morbidity by unbiased interviewers ought to be required. In devising a list of conditions to check, investigators should consult with patients and those clinicians who are most negative about laparoscopy. (See refs #4,p.32; 15,16,p.33.)

RADIOGRAPHY.

In infertility diagnosis, radiography is used essentially only in hysterosalpingography; experts who calculate HSG radiation doses are certain that they are too low for cytotoxic, oncogenic, teratogenic, or genetic effects. The first two are discussed here, the last two, under "SECTION II.

Possible cytotoxic effects on irradiated ovaries might be picked up in studies similar to those described under Ultrasonography, page 88. Oncogenic effects should be demonstrated in such studies as described on pages 88-89, 1) and 2) (Hysterosalpingography). Due to the long latency period in cancer induction (p.35), it is important to find women who had HSGs 20-30 years ago. How many of these women have ovarian, uterine, or bladder cancer? (#5,6,p.36)

FERTILITY DRUG THERAPY.

Each specific drug -- see pages 37 through 45 -- will not be considered separately here because long-term sequelae of each are likely to be similar.

1) Starting immediately there should be a nation-wide study of all cases of ovarian cancer for a statistical analysis of factors in the medical history of each victim. Similarly, ovarian cysts and premature menopause should be analyzed. Such studies should take all cases and then look into correlations.

2) Other studies should follow up each woman who has had fertility drug therapy. Cancer, ovarian cysts, ascites, weight gain, etc. should be surveyed. Menstrual cycle regularity, especially in women who formerly had regular cycles, ought to be tabulated. Particularly important is recording irregularities in previously fertile women -- who had drug therapy because of their husband's infertility, for idiopathic infertility, or to donate eggs.

Symptoms of allergy ought to be noted, particularly in women who plan to return for repeat drug treatments. Allergists should be consulted.

And last but not least, psychological morbidity must be ascertained. What is the frequency of clinical and subclinical postpartum (and other) depression in these women?

ARTIFICIAL INSEMINATION.

To learn more about the true risks of infection to women from AI, physicians who treat women for the diseases listed on p. 58 ought to be enlisted in a nationwide study to ascertain whether each woman presenting with one of those STDs has had artificial insemination. In another approach, 18 months after an AID 'treatment' each woman should be tested for those STDs.

ULTRASONICALLY DIRECTED OOCYTE RETRIEVAL.

Two major confounding factors becloud the issues of quality control and morbidity from methods of UDOR. One is whether the efficacy and safety of a specific method of egg recovery can be separated from the expertise of the team performing it; the other is whether any morbidity may be better ascribed to required fertility drugs, the ultrasound, or anesthesia. Clearly results are poorer and morbidity higher during the learning phase at a clinic.

Nevertheless, the rapid spread of UDOR methods makes carefully controlled and detailed studies imperative to protect American women. Surveys performed by unbiased researchers should cover all the factors listed in the summary on page 65 and include additional negative sequelae suggested by patients themselves.

SECTION II: RISKS TO PROGENY

INTRODUCTION/ ANALYSIS/ IMPROVEMENT OF CURRENT STUDIES.

This discussion will select only those categories of Section I where risk seems most likely, after some generalizations about flaws in current surveys that purport to check whether IVF progeny are normal. Some investigators ask clinics to complete survey forms. In these cases, there seldom are follow-up data on the condition of infants after they leave the hospital. Other researchers study a sample of IVF babies and a control group, using in each case children from only those parents who agree to participate. Wirth et al. (#3,p.95) got 77 families to participate from 100 invitees (from former patients at the Jones Institute for Reproductive Medicine). The families who refuse to participate may be especially important. In my own survey of IVF patients in The Netherlands (#8,p.32), I know almost for certain that the two IVF mothers who refused to complete the questionnaire would have changed the response pattern dramatically.

In IVF newborns, some factors may have been overlooked. For example, has intrauterine growth retardation (IUGR)(light-for-date babies) been always on the checklist? Who does the pediatric examination? Is it a neutral party, not a member of the IVF team? Are both male and female babies examined carefully for compromised genitalia?

Existing tabulations of defects in IVF babies (for example, #3,p.95 and #21,p.81) should be examined carefully for any discrepancies between the types of defects found in cases and in controls. Problematic are situations when there is only one case with a defect in an entire series. For example, in the Wirth study the only case with an undescended testicle in some 150 infants was an IVF baby (#3,p.95); I would predict this as a risk of IVF, but of course, it has no statistical significance. With enough cases, clusters of more frequent defects may emerge.

I recommend controlled studies of sudden infant death syndrome (SIDS) in various sections of the country (to allow for regional differences in frequency) to see whethr SIDS is more common in IVF infants.

Because of the need to follow up IVF children at much later dates, addresses of friends and relatives of all IVF patients ought to be collected.

ULTRASONOGRAPHY.

1) The previous (predating IVF) question of whether obstetric ultrasound is disadvantageous to the irradiated fetus (and/or has any real advantages) needs to be seriously explored. Concerned obstetricians in Great Britain carefully designed a prospective study of the advantages and possible

disadvantages of routine antenatal US imaging. They conducted a very successful pilot study in 1976. However, the Medical Research Council did not provide them the funding for the full study (#27,38 p.18). Funds are provided by the UK National Health Service for purchasing US machines and for sonographer salaries, but not for studying the effects of the technology (#38,p.18). Suggestions have been made that concerned consumers must apply the pressure (and even funding) for such an experiment (#38,p.18).

a) These studies should include cognitive abilities and central nervous system functioning.

b) These studies should be long-term enough to include sexual development in antenatally exposed adolescents.

2) A study should be designed to study US as it is specifically used in IVF with considerable exposure of the ovary.

a) A preliminary study could be swiftly put into place, without raising ethical questions and requiring informed consent, by using existing data banks (such as the one at the National Perinatal Statistic Unit in Australia (#21,p.81)), to see whether any parameters are affected in children born from previously exposed oocytes. [See rationale under (6) on page 13.

b) Studies should be extended to include sexual development in adolescents from US-exposed eggs and early embryos.

HYSTEROSALPINGOGRAPHY and RADIOGRAPHY CONSIDERED TOGETHER.

Are the radiation doses currently used in HSG too low for teratogenic or genetic effects?

1) Evaluate the progeny of women who were pregnant while they had an HSG. True, there aren't many of them, but each case should have been noteworthy and thus easily found in clinic records.

2) Using IVF data banks, such as the Australian one (#21,p.81), separate

IVF progeny from women with HSGs in their infertility workups and those without to determine whether defects are more prevalent in the HSG group.

FERTILITY DRUGS.

1) As described under 'INTRODUCTION' (p.91-92), newborn IVF babies should be examined carefully by pediatrians not involved in IVF programs.

2) In the toddler years ALL IVF progeny ought to be examined for such conditions as autism and failure-to-thrive. There ought to be aggressive pursuit of couples lost to followup, since these two conditions are ones that couples might hide because guilt feelings are often involved.

3) In the early adolescent years IVF children should be examined for anomalies of sexual development.

ARTIFICIAL INSEMINATION.

All AID babies ought to be examined for diseases that may have been transmitted through AID. (See page 59 for list.)

PROGENY FROM FROZEN GAMETES AND EMBRYOS.

My knowledge of biology makes me agree with Schesselman's prediction (#36,p.64) that gametes damaged by freezing simply will not produce embryos so that there will be no child at all rather than a defective one.

Frozen embryos, however, are a different matter. When these are thawed, almost invariably some cells are collapsed, making them partial embryos, since the collapsed cells are inviable. Work with domestic animals has shown that partial embryos can develop into entire organisms, but small at birth. No one, to my knowledge, studied mental abilities of, say, calves from frozen embryos. It is therefore very important to study the babies who develop from frozen embryos. Do they show IUGR? In the postpartum period do they catch up in growth? Do they seem to be compromised mentally in any way?

CONCLUSIONS AND EMPHASES.

What ought to be highlighted in the above list of needed additional research?

If one's goal is to allow more women who want babies to have them, to really help lessen infertility, then the researches grouped under 3) on page 86 should be emphasized. Furthermore, surgeons ought to be extremely careful in all pelvic surgery in women, and should use special care in all infertility treatments with women with previous history of PID or adhesions.

If one's goal is to reduce risks to women from infertility treatments themselves, then one should emphasize the studies under 5) on page 87 and under 2) on page 90.

If one's goal is to protect the children produced by the new reproductive technologies, the emphasis should be on studies of sequelae of fertility drugs, i.e., 1),2),3) on page 94, and frozen embryo babies, page 94.

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RISKS OF INFERTILITY DIAGNOSIS AND TREATMENT

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I. Introduction

The inability of a couple to create a pregnancy results in psychological and often financial difficulties as the man and woman seek a diagnostic and therapeutic answer concerning their childlessness. There is a common belief that fertility can be restored or augmented by simple means, such as the prescription of "fertility pills". In fact, the investigation into the cause of a particular couple's fertility problem may require many tests and several months or even years. The treatment may be as simple as taking a few pills but often involves more complicated therapies. Associated with some of the tests and therapies are potential risks to the health of the man or woman involved. In addition, should a child or children be conceived during or following these tests and therapies, there may be an adverse effect of such interventions on the offspring.

In this report, I will review the nature of the fertility investigation and the treatments which may be useful. Evidence concerning the possible risks to the patient and his/her offspring will be presented. In many cases, there is little evidence or the data are unclear; in such instances I will estimate the likelihood that risks exist. I will not, however, attempt to review the data concerning the efficacy or costs of the tests and therapies discussed. These are important issues and must be used in arriving at a what clinicians like to call a "risk-benefit ratio", but cannot be dealt with adequately in this presentation.

IA. Normal reproductive function

Although there has been much discussion on the issue of when human life begins, pregnancy may be said to commence when the sperm and egg fuse to form a zygote. This event may appear to be a simple matter; however, there are compicated mechanisms which are required in order to form the germ cells, to get them into the right place at the right time, and to provide for nourishment and protection of the conceptus. Detailed discussion of these mechanisms is beyond the scope of this review, but some mention of the processes is necessary in order to understand the rationale behind various fertility tests and treatments.

Gametogenesis is the process by which germ cells are formed. Men and women differ in the timing of germ cell production: in women the full complement of eggs (called ova or oocytes) are in place in the ovaries during fetal life. During the reproductive years, many of the oocytes develop further and one of these is ovulated each month. The oocyte is contained in a structure called the follicle which also includes supporting cells called granulosa cells. These granulosa cells produce estrogens (chiefly estradiol), hormones important in the development of the uterine lining (the endometrium), in the production of cervical mucus, in fallopian tube function, and in hypothalamic/pituitary function. The successful development of a follicle involves proper functioning of the granulosa cells as well as maturation of the ovum. Ovulation requires a coordinated interplay of ovarian and pituitary hormones as well as participation of chemical and perhaps mechanical ovarian factors: Early in the menstrual cycle, follicular maturation and the production of estradiol are stimulated by follicle stimulating hormone (FSH) from the pituitary gland. The amount of estrogen produced by the follicle increases as it matures. When the estrogen level reaches a critical concentration, signifying completion of follicle maturation, the pituitary is stimulated to release luteinizing hormone (LH). Under the influence of LH, the ovum is extruded from the follicle. Following ovulation, the follicle becomes a corpus luteum which produces progesterone. Progesterone further prepares the endometrium for implantation of the conceptus and has other functions during pregnancy.

In men, gametogenesis occurs continuously during the reproductive years. Sperm are produced from precurser cells over a period of approximately two months. The sperm are ejaculated during each coitus. Thus, release of the female germ cell is a carefully orchestrated event occurring about once each month while male germ cells can be delivered on demand.

During coitus, sperm are deposited into the cervical mucus. For a number of preovulatory days, sperm survival appears to be supported by this mucus which serves as a reservoir from which sperm gain access to the upper genital tract. Fertilization normally occurs in the fallopian tube: after ovulation, the ovum is swept into the fallopian tube by the finger-like fimbriae of the tube. Here the ovum encounters a sperm that has reached this location from the lower genital tract. Following fertilization, the zygote undergoes several mitotic divisions within the fallopian tube as it is transported towards the uterus. The resulting conceptus is a rounded ball of cells, called a blastocyst, when it enters the uterine cavity, about six or seven days after ovulation. The blastocyst invades the endometrium, from which it will derive nutritional support, in a process called implantation. Pregnancy will usually be diagnosed a week or more later, when a menstrual period is missed. IB. The approach to the infertile couple

Failure of any of the above processes to occur may result in inability to achieve pregnancy. It should be recognized that repeated loss of an early pregnancy may be regarded as infertility, since although an ovum is fertilized, failure of the pregnancy to survive to implantation and beyond will usually mean failure to diagnose a pregnancy. Thus, if the endometrium is repeatedly unprepared for implantation, the clinical presentation is infertility, although the disorder may more properly be termed habitual early abortion. Other causes of habitual abortion, such as uterine anomalies, result in loss of a pregnancy well after it is diagnosed. The distinction is made because the approach to the patient who repeatedly loses an undiagnosed pregnancy is the same as the approach to the patient who cannot achieve fertilization of an ovum. The evaluation and treatment of habitual abortion of diagnosed pregnancies is different and will not be considered here.

In discussing causes of infertility, it is useful to consider three areas of possible impairment. The first is ovarian dysfunction. This refers to failure of the ovary to ovulate a mature ovum and/or failure to produce adequate hormonal support for the reproductive tract. Anovulation is a common cause of infertility and has a variety of underlying causes. If, for example, there are no ova present in the ovary, ovulation will not occur and the woman will be sterile. If there are ova but they fail to mature and be ovulated, pregnancy will not occur unless induction of ovulation is undertaken. Finally, if ovulation occurs but the resultant corpus luteum makes inadequate levels of progesterone, fertilization may occur, but the conceptus may be lost due to faulty implantation in an unprepared endometrium.

The second area of impairment concerns getting viable sperm into the cervical mucus. Failure to produce adequate numbers of normal sperm may impair fertility as may failure to deposit sperm in the correct location. Even if adequate sperm are placed against the cervix, the cervical mucus may be inhospitable to the sperm, perhaps due to chemical abnormalities of the mucus or due to antisperm antibodies in the mucus. All of these possibilities will result in inadequate access of viable sperm to the upper genital tract of the woman.

The third area is patency of the genital tract. Women with obstruction of the fallopian tubes or, less commonly, with obstruction of the endometrial cavity may fail to permit ovum and sperm to come together or may not provide a way for the conceptus to get to the endometrial cavity for implantation. In the latter case, the conceptus may be resorbed or may implant in an abnormal location (such as within the fallopian tube itself) resulting in an ectopic pregnancy. A woman who has recurring ectopic pregnancies is considered infertile, even though a pregnancy of sorts has been initiated.

Not all cases of infertility fit nicely into one of these three categories. There are a number of instances in which more than one cause of infertility exist together in the same couple. In addition, there are women with endometriosis who are infertile but who have no abnormal findings other than the endometriosis. There is no consensus on the mechanism(s) by which endometriosis may cause infertility, but most clinicians feel compelled to treat this disorder in infertile women in the hopes of improving their reproductive potential.

II. Diagnostic modalities

In the evaluation of an infertile couple, it is customary to perform a number of tests routinely, even though the couple's history and examination may suggest a particular cause of infertility. For ease of discussion, the various tests used will be handled sequentially, roughly in order of their complexity. This is not to imply that the testing should be performed in this order or that all of these tests are appropriate for every individual.

IIA. Tests on the woman

1. Evaluation of cervical mucus

Part of the physicial examination of the woman includes an evaluation of the presence of the genital organs and the function of the ovaries; that is, the presence of signs of estrogenization. The appearance of the cervical mucus is useful in estimating the adequacy of ovarian estrogen production. Under the influence of estrogen, the mucus becomes clear, abundant, and stringy. These changes are maximal just prior to ovulation. Examination after ovulation will not permit this sort of evaluation; under the influence of progesterone the mucus diminishes in amount, becomes cloudy, and becomes tacky. There are no data on possible risks of cervical mucus evaluation, neither are their likely to be risks associated with this procedure.

A refinement of mucus examination is examination after the couple has had coitus. Such an examination, called a postcoital test or a Sims-Huhner test, is timed for the anticipated preovulatory period. Mucus is evaluated for adequacy of estrogen effect as well as for the presence of motile sperm. There are no known risks of this procedure and it is not expected that this procedure would be harmful.

2. Genital canal patency tests

Tubal insufflation: An older test for the presence of a patent canal between the cervix and the peritoneal end of the fallopian test was developed by Rubin and bears his name. The Rubin test involved placing a canula into the cervix and insufflating gas (usually carbon dioxide) under low pressure. Although theoretically an obstructed fallopian tube might be ruptured by the insufflation of gas, there are no data suggesting how often this might occur. The test has largely been abandoned because more accurate methods of evaluation are available.

Hysterosalpingography: A modification of the Rubin test is the injection of radioopaque material through the cervical canal and observation of the flow of this dye with fluoroscopic control. This hysterosalpingogram (HSG) will outline the uterine cavity and the lumina of the fallopian tubes. If the genital canal is patent, the dye will spill into the peritoneal cavity. If the canal is obstructed, the location and perhaps the nature of the obstruction can be identified.

The major risk to the woman of HSG is the spread of microorganisms from the cervix to the upper genital tract and/or the reactivation of dormant pelvic organ infection. In a series of 231 women undergoing HSG, two developed signs of acute pelvic infection after the procedure for a major complicatin rate of 0.9% (Rice et al, 1986). Women with a history suggestive of pelvic infection in the past may be at increased risk of this complication, with febrile morbidity as high as 3% in high risk women (Stumpf and March, 1980). Some authorities recommend the use of prophylactic antimicrobial agents around the time of HSG; after a protocol using doxycycline prophylaxis, one group was able to reduce its rate of infectious complications of HSG to zero (Pitway et al, 1983). It has been wondered whether HSG procedures might spread endometrial tissue to the perioneal cavity, resulting in endometriosis. Such an occurrence has not been shown. An additional risk, however, of HSG is access of the radioopaque contrast to the intravascular space. When this occurs witn water-based contrast media, there is unlikely to be a problem. Oil-based contrast, however, may embolize to the lung and cause respiratory distress. With careful fluoroscopic control of the procedure, however, this complication is unlikely. Finally, hypersensitivity to contrast material may occur. The nature of this complication is similar to that encountered with other radiologic procedures.

Whether there is risk to the offspring from HSG is unknown. There is concern about radiation exposure of an early embryo; however, the dose of radiation from HSG is on the order of 1 rad or less. This amount of radiation appears unlikely to result in an increase in adverse pregnancy outcome (Lione, 1987). Whether or not an HSG can dislodge an implanted blastocyst is unknown but this possibility appears unlikely. In order to avert any theoretical risks to the early embryo, the HSG procedure is customarily performed prior to the anticipated time of ovulation.

Laparoscopy with chromopertubation: Laparoscopy is a surgical procedure in which a small telescope is inserted into the abdominal cavity for visualization of pelvic organs. It is customary for the scope to be placed through an incision in or near the umbilicus. Often one or more incisions are made just above the pubic region for placement of additional instruments to assist in movement, measurement, and/or biopsy of intraabdominal structures. Placement of a cannula in the cervix permits injection of a visible dye through the genital canal while the laparoscopist observes for spill of the dye from the intraabdominal ends of the fallopian tubes. This procedure, called chromopertubation, is similar to the HSG in the information provided; although the HSG yields better information about the uterine cavity and the inner contour of the genital canal and the laparoscopy is more useful for determining the nature of genital canal obstruction. It should be recognized that laparoscopy is useful in a number of other clinical settings, many of which do not involve fertility evaluation and treatment. One of the most common indications for laparoscopy is female sterilization by tubal cautery or banding. Many of the data on the incidence of adverse outcomes from laparoscopy have been collected in populations undergoing laparoscopy for a variety of indications; however, these data may be used to estimate the risk from the use of this operation for infertility evaluation.

All surgical procedures have the potential for complications. Of these, infection is one of the more common. The large number of laparoscopic procedures appearing on the schedule of many operating rooms has led to the practice of disinfecting the laparoscope equipment between cases rather than using more time-consuming sterilization techniques. This has raised the issue of whether increased rates of infection might occur due to this practice. In a review of more than 10,000 laparoscopies in which disinfection was used instead of sterilization (Loffer, 1980), there were no cases of post-operative sepsis. Most other reports, however, indicate an infection rate above zero, although none have established a relationship between disinfection techniques and an increased rate of infection. A low infection rate was reported from a community hospital in which 7270 cases were followed by three instances of peritonitis and two intraabdominal abscesses, for an overall infection rate of 0.7 per 1000 cases (Edgerton and Kleppinger, 1977). More typical appear to be infection rates of two to three per thousand (Baggish et al, 1979; Phillips et al, 1977; Penfield, 1985). Of these, most infections are superficial, involving the incisions in the abdominal wall. Intraabdominal infection, such as abscess of the mesosalpinx, appears more likely to occur with an operative intervention such as tubal cauterization.

Other risks associated with laparoscopy include injuries to intraabdominal organs. These are associated in diagnostic procedures with introduction of instruments through the abdominal wall. In conventional laparoscopy, the initial step in the operation is the establishment of a pneumoperitoneum; that is, the placing of two or three liters of gas (often carbon dioxide or air) into the peritoneal cavity. This gas lifts the abdominal wall off the viscera permitting more space for insertion of instruments and a clearer view of the intraabdominal contents. The placing of the gas is often accomplished with a long needle, placed blindly into the abdomen. Placement of the needle into intestinal or vascular structures may be associated with severe injury to these organs and the need for major surgical repair. In a survey of the members of the Americal Association of Gynecologic Laparoscopists in 1976 and again in 1979, major complications such as these were reported to occur in 2.7 per thousand and 1.8 per thousand cases (the lower number perhaps reflecting greater experience with the procedure by the time of the second survey). There were three operative deaths in 77,103 procedures in 1976 and 2 deaths in 88,986 procedures in 1979, for death rates of four per hundred thousand and two per hundred thousand respectively (Phillips et al, 1981). In an attempt to eliminate the risks associated with blind placement of the needle, some practitioners use an "open" tecnhique, wherein a small incision near the umbilicus is developed in layers under direct visualization. The peritoneal cavity is entered under full vision and a sleeve placed with a blunt trocar or with no trocar at all. The gas, and subsequently the laparoscope, are placed through the sleeve. It might appear that the open technique must be safer than the closed; however, there have been few studies comparing the two. Penfield's uncontrolled report on just under 11,000 open procedures yielded what appears to be a low incidence of bowel injury of 0.6 per thousand (Penfield, 1985). A comparison of open and conventional techniques by the same investigators showed an identical rate of complications (most of which were minor) of 1.4% (Bhiwandiwala et al, 1985). The authors correctly point out that the incidence of major blood vessel or visceral injury is so low by either technique that it will be difficult to prove the advantage of one over the other. Certainly, the presence of aberrant large vessels in the abdominal wall (Salmi, 1986) or adhesions of bowel to the periumbilical region will predispose to serious operative injury from either technique.

In laparoscopic procedures where intraabdominal surgery is performed, another opportunity for visceral injury exists. The complication of this type most commonly encountered has been thermal injury to the intestine during coagulation of the fallopian tubes for sterilization. Such bowel burns occur in 0.5 to 3.2 per 1000 cases (Cusonan, 1980). Although tubal cautery is not used in infertility patients, it should be appreciated that the use of cautery and cutting instruments on intraabdominal adhesions may be employed during a laparoscopy for infertility. Thus, the patient may be exposed to injury of this type. There are, however, no data on how often such injuries occur exclusively during infertility work.

A final source of complications during laparoscopy is the gas used to lift the anterior abdominal wall from the viscera. Gas-related shoulder discomfort after surgery is common, but serious complications are rare. There have been case reports of hydropneumothorax, presumably from transdiaphragmatic migration of gas (Ramage et al, 1986), and of fatal carbon dioxide embolism (Gomar et al, 1985). Gas emboli may be associated with exceptionally large volumes or pressures of insufflated gas or with accidental insufflation into a vessel. Laparoscopy without the use of pneumoperitoneum has been reported to be safe and practical for sterilization procedures (Saidi, 1986); however, the limited view permissible without gas might not be appropriate for an infertility evaluation.

Of interest is one report in which periovulatory laparoscopy was used in monkeys. The pregnancy rate in operated animals was 22.3% compared to 38.3% in non-operated controls (Eddy et al, 1986), suggesting that laparoscopy exerts a negative effect either on fertility or on viability of the early embryo. It is not known whether these findings are applicable to humans, especially since the effect has not been shown to extend beyond the cycle of surgery.

Hysteroscopy: A telescope may be inserted into the uterine cavity in order to visualize possible anatomic abnormalities of this portion of the genital canal. The infertility problem most commonly assessed with hysteroscopy is Acherman's syndrome, which consists of intrauterine scarring, sometimes to the point of obliterating the entire uterine cavity. Hysteroscopy may also be used to evaluate submucosal leiomyomata ("fibroids") and intrauterine septa, although these problems are not usually associated with infertility. The hysteroscope may also be used in the therapy of intrauterine disorders. Thus, intrauterine scar tissue may be resected through the scope. As is the case for laparoscopy, the data on complications of hysteroscopy generally include all cases (purely diagnostic as well as interventional procedures).

Hysteroscopy procedures are divided into two types. Contact hysteroscopy involves placement of the end of the telescope very close to or in contact with the structure being observed. This is necessitated by the short focal length of the instrument. Panoramic hysteroscopy utilizes an instrument with a wider angle, longer focal length lens and gives a larger picture of the uterine cavity. It is not necessary to review the different indications for each procedure; suffice it to say, the panoramic modality is the technique almost always used for infertility patients. Panoramic hysteroscopy requires that the walls of the uterus be separated by a distending medium. This is a gas or a liquid. Carbon dioxide and nitrous oxide are the most commonly used gas media. The liquids used include dextran, saline, and dextrose or glucose solutions.

Complications of hysteroscopy may be attributable to this distending medium. Carbon dioxide can cause hypercarbia, acidosis, and cardiac arrhythmias (Quinones, 1984), although a review of 1500 cases in which carbon dioxide was used showed no complications and there were no changes in pH, pCO2, or electrocardiogram in 40 monitored patients (Lindemann, 1974). Nitrous oxide delivered under constant pressure without control of volume may cause hypercarbia and cardiovascular collapse (Hulf et al, 1979). No change in pCO2 was noted in the same study when carbon dioxide was given using a constant volume device. In their review on hysteroscopic technique, Taylor and Hamou (1983) emphasize that special equipment for regulating gas flow is necessary for hysteroscopy since large volumes of gas (30-40 liters) may be fatal. A flow rate of 40-60 ml/min appears to be safe for this procedure. Dextran is a very popular distending medium but is not without potential complications. Anaphylactic reactions to this agent are unusual, but were reported in 1 in 100 patients in one series (Taylor and Cumming, 1979). Subsequent experience of this group enabled a revision of the incidence of this complication to 1 in 1000 cases (Taylor and Hamou, 1983). The use of dextran, especially in large volumes, may also be associated with substantial intravascular absorption with pulmonary edema and coagulopathy. Another unusual complication of the distending medium is rupture of an obstructed fallopian tube (Siegler et al, 1975; Taylor and Hamou, 1983).

The insertion of instruments into the uterus introduces the possibility of perforation of the uterus. This occurs infrequently in diagnostic procedures. In a series of 5200 diagnostic procedures, perforation was recognized six times for a complication rate of 0.1%. The use of the hysteroscope to perform intrauterine surgery increases the risk of perforation. In one series of hysteroscopic procedures, the perforation rate was 2% (Siegler et al, 1976), while in 66 patients who underwent operative hysteroscopy for intrauterine adhesions, perforation occurred twice for a rate of 3% (March et al, 1978). Because intrauterine surgery is more likely to be accompanied by perforation, it is customary for a second operator to keep the external aspect of the uterus under surveillance with a laparoscope when hysteroscopic surgery is performed. Pelvic infection after hysteroscopy is also unusual although the incidence of this complication appears to increase in interventional procedures (Amin et al, 1983; Taylor and Hamou, 1983).

Pregnancy problems attributable to hysteroscopy are difficult to identify since many women subjected to this procedure have uterine abnormalities to begin with. Placenta acreta (an abnormally invasive placental insertion) has been reported after hysteroscopic lysis of intrauterine scars (Georgakopontos, 1974), but could clearly have been due to the abnormal uterine lining rather than to the operative procedure. In 20 pregnancies occurring after hysteroscopic lysis of intrauterine adhesions, Amin and coworkers (1983) found no cases of placenta acreta although one patient had postpartum uterine atony. In another group of 122 women treated with hysteroscopy for intrauterine adhesions, polyps, leiomyomata, or foreign bodies, there were 55 pregnancies. Of these, one was an ectopic pregnancy, eight miscarried, and 46 went successfully to term (Valle, 1984). Although a control group was not reported, these figures are not inconsistent with the expected incidence of adverse pregnancy outcome.

3. Tests of ovulation and luteal function

The evaluation of the function of the ovary consists, broadly speaking, of determining whether a follicle is matured to the point of ovum release and whether the hormone-producing capability of the follicle (and the corpus luteum which it becomes) is normal. These two aspects of ovarian function are closely related: follicle development and ovulation are invariable predecessors of normal luteal function. If ovulation fails to occur, normal luteal function cannot be expected. Normal ovulation may, however, be followed by abnormal luteal function.

The only proofs of ovulation are pregnancy (which obviates the need for an infertility evaluation) and recovery of the ovum from the genital tract (which is impractical). Practical tests of ovulation are, therefore, presumptive rather than conclusive. These tests are, in fact, reflections of luteal function rather than of ovulation itself.

Basal body temperature measurement: The production of progesterone by the corpus luteum results in a shift upward of the resting body temperature. Detection of this shift with a sensitive thermometer suggests exposure to progesterone and, therefore, ovulation. There are no known risks associated with measuring basal body temperature and none are considered likely.

Progesterone measurement: Blood or serum progesterone measurement is available in many commercial laboratories. Measuring hormone levels every two or three days enables the construction of a graph of progesterone levels. This permits an evaluation of the adequacy of luteal function and, retrospectively, evidence of ovulation. There are no known or likely risks associated with these measurements.

Endometrial biopsy: One of the functions of progesterone is to change the lining of the uterus in order to permit implantation and nourishment of the conceptus. These progesterone-induced changes are identifiable using light microscopy and, further, the degree of change correlates with the amount or duration of exposure to progesterone. It is possible, then, to examine the uterine lining (the endometrium) to determine whether there has been progesterone exposure appropriate for the presumed date of ovulation, which may be determined using basal body temperature measurements. Inadequate progesterone effect is one of the criteria used to define luteal phase deficiency (LPD), which is presumably due to inadequate function of the corpus luteum in spite of ovulation having occurred. Endometrial biopsy is an office procedure in which a small instrument is placed through the cervix and used to suction or scrape off a sample of tissue. Perforation of the uterus with the biopsy instrument is a potential risk of this procedure as is the introduction of infection into the genital tract. There are no data with which to estimate the frequency of these complications, but both are believed to be uncommon. Endometrial biopsy is an uncomfortable procedure, but the duration of the discomfort is brief.

Since endometrial biopsy is performed after ovulation but before the onset of a menstrual period, it is possible that the biopsy will be performed in a uterus with an early pregnancy. One report found this to have occurred in 20% of cases (Jacobson and Marshall, 1980), although 1-4% is a much more commonly reportedly incidence of this complication (Buxton and Olson, 1969, Karow et al, 1971; Wild et al, 1986; Wentz et al, 1986). An early paper on biopsy during the cycle of conception found that in 18 such pregnancies, all were delivered of viable infants (Wilson et al, 1966). Other authors give abortion rates as follows:

Rosenfeld and Garcia, 1975	6%
Karow et al, 1971	7%
Arronet et al, 1973	9%
Jacobson and Marshall, 1980	14%
Wentz et al, 1986	17%
Sulewski, 1980	22%
Wild et al, 1986	22%
Balasch et al, 1984	32%

The small number of cases in each series almost certainly accounts for the apparently large differences among abortion rates. The attitude of different authorities towards biopsy in the cycle of conceptions appears to depend on the statistics in the individual authority's institution. For example, Wild et al (1986) conclude that the 22% miscarriage rate after endometrial biopsy in pregnancy in their patients is not different from the background miscarriage rate in other infetility patients. Balasch et al (1984), on the other hand, conclude that endometrial biopsy during early pregnancy clearly increases the risk of abortion. Wentz and her coworkers (1986) very carefully evaluated the outcome of the biopsies in 54 early pregnant uteruses. Of the nine who spontaneously aborted, one contained a trisomic embryo, which certainly would not have survived. Only one biopsy of the nine contained an implantation site. In continuing pregnancies, normal outcome is the rule; that is, damage to the surviving embryo has not been noted after endometrial biopsy during pregnancy.

Three studies have noted ectopic pregnancies after endometrial biopsy in the cycle of conception. Karow et al (1971) and Wentz (1980) noted one each. The 1986 series by Wentz et al reported 2 ectopics. The small numbers do not permit an estimate of whether the risk of ectopic pregnancy is increased by endometrial biopsy in the cycle of conception. On theoretical grounds, the risk should not be increased since the biopsy is performed several days after implantation in the uterus or the tube has occurred.

In summary, endometrial biopsy is a briefly uncomfortable but generally safe procedure. Biopsy during the cycle of conception may result in spontaneous abortion, but the likelihood of this complication does not appear in most series to be increased over the baseline risk of miscarriage in early pregnancy (which is about 20%). Damage to a surviving embryo and an increased risk of ectopic pregnancy are not believed to occur in association with this procedure.

4. Tests for endometriosis

Although the mechanism by which endometriosis may cause infertility is unclear, the presence of this disorder is often suspected in infertile women, especially if no other cause of the infertility is evident. Classical symptoms and physical signs of endometriosis may not be present in women who have significant disease; hence, diagnostic modalities other than history and physical examination may be necessary.

Ultrasound: The use of sound energy to generate an image dates back to the development of sonar used for locating submarines. Ultrasound equipment has become increasingly sophisticated and the association of sensitive transmitter-receiver crystals with powerful computers now permits visualization in detail of many structures within the body. Ultrasound examination cannot diagnose endometriosis with certainty but may suggest its presence.

The safety of ultrasound has been studied most extensively with regard to use of the technique during pregnancy (Fabro et al, 1984). The amount of energy transmitted to biologic tissues from diagnostic ultrasound is extremely small and the risk of damage to these tissues is considered to be negligible. There is, in fact, no convincing evidence that obstetrical ultrasound is harmful to the embryo or fetus.

There are fewer data, however, on ultrasound effects on the ovary or the developing follicle. These are the structures of interest which would be insonated during an evaluation for endometriosis. Exposure of mouse ova to ultrasound prior to in vitro fertilization does not produce deleterious effects (Puissant et al, 1984). In humans, ultrasound exposure of the developing follicle has been used to assist in timing artificial insemination procedures. In the experience of two groups, the use of ultrasound in this setting has improved pregnancy rates (Marinho et al, 1982; Kerin et al, 1980). Such an improvement would not be expected if the ultrasound examination were harmful to the ova or to the reproductive organs. There is, however, one paper in which the success of artificial insemination cycles is reported to be decreased by the use of ultrasound (Demoulin et al, 1985). These investigators noted after three months of insemination that the use of clinical criteria alone for the timing of insemination was associated with a 71% success rate while the addition of ultrasound criteria was associated with a 17% success rate. On evaluating the pregnancy rates month by month, however, the groups differ only in their first month pregnancy rates. Success rates in subsequent months were similar, regardless of whether or not ultrasound exposure occurred. These data suggest that other factors (such as mistiming of insemination) may have been responsible for the poorer success of insemination during the first month in the ultrasound-exposed subjects. In the same paper, preovulatory exposure to ultrasound in female rats is reported to reduce the litter size (from 13.84 to 11.09) compared to unexposed controls. There was no difference between the groups in ovarian histology or in the number of oocytes released per cycle, casting some doubt on the significance of the findings.

Laparoscopy: Direct visualization of the pelvic organs is the most reliable method of diagnosing endometriosis. This is accomplished with laparoscopy. The risks associated with this procedure are discussed above.

Scialli - Part 3 of 9 IIB. Tests on the man 1. Semenalysis

The examination of semen for sperm concentration, motility, morphology, and other parameters is the main test used in evaluating male fertility. Specimens are ordinarily collected by masturbation. There are no known hazards to this examination and it is not believed to be a risky procedure.

2. Testicular biopsy

Examination of testicular tissue is possible through removal of a small piece of the testis. This is a minor procedure. Although bleeding and infection are possible complications of all surgical procedures, they are not considered prominent complications of testicular biopsy. There has been concern, however, that removal of testicular tissue may impair fertility. In healthy rats, removal of testicular tissue by biopsy is associated with a transient decrease in fertility in proportion to the amount of tissue removed (Consentino et al, 1986). This effect is not seen after removal of one entire testis, suggesting that testicular biopsy results in subtle vascular injury with global impairment of testicular function. In this study, however, up to 30% of the rat testis was removed compared to well under 1% in human biopsies. In a study on 20 healthy human volunteers, testicular biopsy resulted in a decrease in sperm concentration in 9 (45%). There was, however, no long term follow-up in this group. Another study of biopsy in 100 healthy men showed a transient decline of sperm count in 40%. All recovered within 18 weeks. Although these data are reassuring, they do not establish that testicular biopsy is a benign procedure. It is possible that biopsy of a testis that is already impaired might lead to more permanent adverse consequences. There are no data with which to evaluate this possibility and the general practice of andrologists is to withhold testicular biopsy unless there are compelling reasons to perform the procedure.

3. Vasography: Injection of radiologic contrast material into the vas deferens has been used to visualize portions of the male genital duct system (comparable to HSG in the female). This procedure is generally avoided, however, due to the possibility of injury to the vas or epididymis (Ross, 1983).

III. Therapeutic modalities

The therapies used in treating infertility are based on the diagnosis of the cause of the fertility problem. It should be recognized that there are practitioners who recommend various therapies for unexplained or inadequately explained infertility. Internal spermatic vein ligation may, for example, be advised for a man with oligospermia of unknown cause. Although there has been much written about the empiric use of therapies for incompletely diagnosed fertility problems, this discussion will deal only with possible risks of treatment, without regard to the strength of the indications of the treatments in the first place.

IIIA. Ovulation induction

Stimulating the ovary to ovulate involves more than getting the ovum to physically pop out of the follicle. Ovulation induction virtually always involves stimulation of follicle and ovum maturation and is therefore a process which occupies much of the first half of the monthly female reproductive cycle. Ovulation inducing agents include clomiphene citrate

(CC), gonadotropins, and gonadotropin releasing hormone (GnRH). CC is an antiestrogen which displaces endogenous estrogens from receptors in the central nervous system, thereby increasing the production of gonadotropins. Gonadotropin therapy involves administering these same gonadotropins exogenously. Originally, the gonadotropins were of human pituitary origin; however, harvesting human pituitaries and extracting hormones is expensive. Currently, a popular source of gonadotropins is the urine of menopausal women, giving rise to a preparation called human menopausal gonadotropins (HMG). HMG contains both FSH and LH. Purified FSH is also available. If LH activity is desired, it is customary to give human chorionic gonadotropin (HCG), a placental hormone which is very similar in structure and function to LH. GnRH has recently been introduced in fertility therapy. This agent stimulates endogenous FSH and LH release. A final agent for ovulation induction is bromocriptine. This ergot derivative acts to decrease prolactin production by increasing central dopamine activity. In instances where elevated prolactin levels are present, anovulation may be the result of decreased gonadotropin production and/or decreased ovarian responsiveness. A return of the prolactin towards normal may result in disinhibition of the normal mechanisms of ovulation.

1. Clomiphene citrate: CC is customarily given daily for five days during the early days of the menstrual cycle. The central nervous system estrogen receptor blockade results in increased production of FSH with enhanced follicle maturation and endogenous estrogen production. When the CC is withdrawn, the increasing levels of estrogen are recognized by the now unblocked central receptors, an LH surge is triggered, and ovulation occurs. The estrogen receptor blockage of CC involves not only the central nervous

system, but peripheral estrogen receptors as well. This causes concern that other estrogen-dependent events in the reproductive tract may be adversely influenced by CC treatment. CC treatment, for example, might result in subadequate cervical mucus, impaired tubal motility, or abnormal sperm transport. The observation that the 70-90% ovulation rate with CC is much higher than the 30-40% pregnancy rate with this agent supports the belief that CC exerts adverse effects on some of these aspects of reproduction (Wu, 1984). It is widely believed that CC is capable of causing LPD (Cook et al, 1984; Garcia et al, 1977). Based on work in monkeys by Marut and Hodgen (1982), a mechanism for CC induction of LPD has been formulated. During follicle maturation, gonadotropin receptors are synthesized under the influence of estrogen. In the presence of estrogen receptor blockade by CC during the early days of follicular maturation, synthesis of gonadotropin receptors may fail to occur. This deficit in gonadotropin receptors may not be corrected, even after CC is withdrawn, resulting in decreased responsiveness of the follicle, and subsequently of the corpus luteum, to gonadotropins. Although this hypothesis is plausible, it cannot be regarded as proven. In addition, it is not know how often evidence of LPD may be found in the cycles of normal, fertile women. Without this sort of control information, it cannot be established that women on CC therapy have a significantly increased incidence of LPD.

The need for adequate control information is especially clear when considering whether CC induction of ovulation increases the likelihood of spontaneous abortion. It was at one time widely believed that infertility patients in general have a higher incidence of miscarriage than do normal women; however, this is almost certainly due to the greater surveillance of infertility patients. For example, a woman who is keeping track of basal body temperatures and has a pregnancy test at the first hint that she may have conceived will be diagnosed earlier as pregnant than a woman who is not paying as much attention to her reproductive status. If a woman with an early positive pregnancy test bleeds and converts her pregnancy test to negative, she will be diagnosed as having aborted. If the same episode occurs in a woman who does not realize that she is pregnant, she may consider the bleeding to be a late menstrual period and think nothing more of it.

Studies with adequate controls are divided in their findings on abortion in pregnancies conceived after CC. Two reports have found CC pregnancies about 2.5 times more likely to miscarry than spontaneously conceived gestations (Garcia et al, 1977; Toshinobu et al, 1979). Two other groups found no difference in miscarriage rates after CC or after spontaneous ovulation (Adashi et al, 1979; Kurachi et al, 1983). If CC causes an increased rate of early pregnancy loss, it is probably due to impaired luteal function, as discussed above. The idea that embryos conceived after CC induction of ovulation are defective was suggested by animal studies using high dose exposures, but this conclusion cannot be supported by the many normal human embryos obtained for in vitro fertilization after CC stimulation of ovulation (Dlugi et al, 1985).

There are isolated reports of other complications associated with CC-induction of ovulation. A woman was reported, for example, to have had four consecutive molar pregnancies, three of which were conceived after CC and one after HMG (Mor-Joseph et al, 1985). The lack of control data makes this observation interesting but not informative. Mild hyperstimulation, consisting of ovarian enlargement, may be seen in up to 13.5% of women after CC treatment (Kistner, 1975) but is usually of no significance and resolves spontaneously. Of perhaps more importance is a possible increase in ectopic pregnancy after CC-induced ovulation. The incidence of ectopic pregnancy in the United States is about 1.4% of reported pregnancies (Centers for Disease Control, 1986). A series of 249 CC-induced pregnancies reported an ectopic incidence of 2% (Corson et al, 1983). In a retrospective survey of 274 women with ectopic pregnancies and 548 women who delivered normally at term, five of the ectopic patients were found to have conceived after CC compared to one of the normal patients. This yielded a relative risk of 10; however, the confidence interval was large (1.8-56.8) (Marchbanks et al, 1985). If CC use is associated with an increased risk of ectopic pregnancy, this may be due to alterations in tubal motility, to a higher incidence of damaged tubes in infertile women (who tend to get placed on drugs such as CC), or to the increased number of ova released after ovulation induction, increasing the number of opportunities for a tubal implantation (Corson and Batzer, 1986).

The most important adverse consequence in pregnancies conceived after CC is the increased incidence of multiple gestations, which are almost exclusively twins. Rates of multifetal pregnancies after CC have been reported as 8-13% (Adashi et al, 1979; Macgregor et al, 1968; Harlap, 1976; Hack et al, 1972; Karow and Payne, 1968). Twinning imposes a high risk of several pregnancy complications including prematurity, gestational diabetes mellitus, toxemia, and placental abnormalities. It is not believed that these complications are likely to occur more often in CC-induced twin pregnancies than in spontaneous twin pregnancies, although this possibility has never been studied. There are several uncontrolled reports suggesting that the incidence of birth defects in children born after CC induction is no higher than in the general population (Macgregor et al, 1968; Harlap, 1976; Hack et al, 1972; Karow and Payne, 1968; Lee et al, 1982; Ahlgren et al, 1976). One prospective controlled study confirms the similar incidence of birth defects in CC and spontaneous pregnancies (Kurachi et al, 1983). Follow-up evaluation of children born following CC showed no problems in growth over the first year of life (Hack et al, 1972).

2. Gonadotropins: Most of the published literature on gonadotropin induction of ovulation concerns HMG. It is usual to give increasing doses of HMG by injection, beginning early in the menstrual cycle and stopping when a key level of estrogen is measured in blood or urine and/or when an adequate follicle is visualized by ultrasound. HCG is then injected as a surrograte for the LH surge.

As reported for CC, HMG treatment may be associated with LPD (Olson et al, 1983; Dlugi et al, 1984); however, this appears to be an unusual occurrence and pregnancy rates in women ovulating on HMG therapy are very high. These women are, however, at risk for ovarian hyperstimulation syndrome (OHSS). OHSS has been well-summarized by Diamond and Wentz (1986). Features of this syndrome include ovarian enlargement, which may be massive, abdominal distension with ascites and/or hydrothorax, and hemoconcentration with an increase in blood viscosity and coagulation abnormalities, including thromboembolism and death (Mozes et al, 1965; Schenker and Weinstein, 1978). OHSS is largely the result of excessive HMG administration and can usually be avoided by careful monitoring of blood estrogen levels. Administration of HCG appears to be required for the production of OHSS (Schenker and Weinstein, 1978); therefore, if estrogen levels are found to have become too high, the HCG can be withheld. OHSS also appears more common in cycles where pregnancy has occurred (Haning et al, 1983). It has been estimated that mild OHSS occurs in up to 23% of HMG cycles, moderate OHSS in about 7%, and severe OHSS in 0.8-2% (Schenker and Weinstein, 1978).

Data on the incidence of spontaneous abortion in HMG-induced pregnancies is difficult to interpret due to the inclusion of hyperstimulated cycles, with their poorer outcome, in the older studies. Controlled studies have not, in general, identified an increase in miscarriage attributable to HMG therapy (Kurachi et al, 1983; Ben-Rafael et al, 1983). Ectopic pregnancy rates of 2.7% (Gemzell et al, 1982) and 3.1% (McBain et al, 1980) have been noted in HMG-induced pregnancies. Of particular interest is the finding of a 12.5% ectopic rate in pregnancies conceived after hyperstimulation (McBain et al, 1980), lending support to the hypothesis that tubal motility is adversely affected by high estrogen levels.

Multiple pregnancies are more commonly encountered after HMG therapy than after CC. Twin and higher order pregnancies occur in 11-42% of HMG-induced gestations (Harlap, 1976; Caspi et al, 1974; Marshall and Wider, 1971; Schwartz et al, 1980; Hack et al, 1970; Spadoni et al, 1974). Triplets occur in 5-6% of HMG pregnancies (Caspi et al, 1974; Schwartz et al, 1980; Hack et al, 1970). The incidence of multifetal gestation appears related to the care with which estrogen levels are monitored and a rate as low as 10% may be obtainable (March, 1984). Nearly all the pregnancy complications occurring in HMG pregnancies are attributable to multiple gestation and attendant prematurity and perinatal death.

Birth defects do not appear to occur more commonly in children born after HMG therapy (Harlap, 1976; Hack et al, 1970; Spadoni et al, 1974; Kurachi et al, 1983). Growth and development during the first year of life are normal in these children (Hack et al, 1970).

Bromocriptine: Use of bromocriptine to restore ovulatory function in hyperprolactinemic patients has become common. Bromocriptine also has been continued during pregnancy in a few patients with pituitary adenomas and/or acromegaly.

Many individuals taking bromocriptine experience side effects such as nausea, hypotension, hair loss, and headache (Brion et al, 1985; Dewailly et al, 1985). More serious complications of therapy have occassionally been reported, including pleuropulmonary fibrosis (Wiggins and Skinner, 1986; Rinne, 1981; Lewitt and Calne, 1981; Bottcher and Gron, 1981; Vergeret et al, 1984) which occurs with some regularity in patients on bromocriptine for extended periods of time, as in the treatment of Parkinsonism. Psychosis has been reported to have been induced by bromocriptine (Taneli et al, 1986; Johnson, 1981; Vlissades et al, 1978; Brook and Cookson, 1978), ostensibly due to effects on central neurotransmitters. A case of pituitary apoplexy in an acromegalic treated with bromocriptine has been reported (Alhajje et al, 1985). Although the mechanism for this is unknown, the possibility exists that in patients with adenomatous or hyperplastic lesions of the pituitary, bromocriptine may induce abrupt vascular insufficiency of the gland. Of particular concern are reports of stroke (Katz et al, 1985) and myocardial infarction (Iffy et al, 1986) in young, apparently healthy women on moderate doses of bromocriptine. It is believed that these complications may be due to an increase in coagulability of blood and, in fact, women over 25 years of age appear to have about a ten-fold increased risk of thromboembolic events when on bromocriptine (Daniel et al, 1967).

Although controlled studies are lacking, the success of pregnancies conceived after bromocriptine therapy appears similar to that of spontaneous ovulation. Many of the reports on this issue include patients in whom bromocriptine was stopped as soon as pregnancy was diagnosed, but some include cases in which bromocriptine was continued throughout gestation. Due to the small number of patients who take this drug throughout pregnancy, it is not possible to analyze this sort of exposure separately. The rates of spontaneous abortion, ectopic pregnancy, and molar pregnancy after bromocriptine appears similar to those in the general population (Turkalj et al, 1982; Molitch and Reichlin, 1982). The incidence of multiple gestation (almost exclusively twins) is 1.2-1.8%, which does not appear higher than in the general population (Ruiz-Velasco and Tolis, 1984; Turkalj et al, 1982; Molitch, 1982). Pregnancies conceived after bromocriptine therapy do not appear to be at increased risk for preterm delivery, abnormal antepartum and postpartum growth, or birth defects (Bigazzi et al, 1979; Ruiz-Velasco and Tolis, 1984; Turkalj et al, 1982; Yuen et al, 1982; Canales et al, 1981; Luboshitzky et al, 1980; Konopka et al, 1977; Molitch, 1982; Randall et al, 1982; Weil, 1986).

Other prolactin reducing drugs have been developed in an attempt to treat hyperprolactinemia without the troublesome side effects of bromocriptine. These drugs are all either dopamine agonists or seritonin antagonists and include mesulergin (Dewailly et al, 1985), cyclofenil (Cingotti and Magnin, 1986), metergoline (Casson et al, 1985), and terguride (Dallabonzana et al, 1985). To date, none has been shown clearly better than bromocriptine. Data on possible adverse effects of these agents are limited.

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4. Gonadotropin releasing hormone: The use of GnRH for ovulation induction is a new technique. The drug is given in pulses using a pump connected to a subcutaneous needle or cannula. A minor complication of this technique is infection at the site of the needle or cannula insertion (Hurley et al, 1984). When the technique was developed, it was believed that it would offer the good success rate of HMG therapy without the risk of OHSS; however, minor hyperstimulation has been reported using GnRH (Skarin et al, 1982; Lorcy et al, 1984; Liu et al, 1983; Burger et al, 1983). In addition, a case of quadruplets has occurred after GnRH induction (Heineman et al, 1984). At the present time, the technique is too new for an evaluation of possible complications; however, it is expected that these will be similar to those encountered with HMG therapy, although probably occurring less often.

IIIB. Luteal phase support

As discussed above, LPD involves failure of the corpus luteum to make adequate progesterone. Many workers now believe that an inadequate luteal phase is indicative of poor follicular development, as discussed above with regard to CC-associated LPD. One approach to the treatment of LPD, therefore, is the use of ovulation inducing agents to improve the maturation of the preovulatory ovum. The most direct therapy of LPD, however, involves the administration of progesterone itself, usually in a vaginal suppository.

The literature on progesterone safety is often difficult to interpret due to a tendency, especially in early papers, to refer to all progestins as "progesterone". Progestins include a group of agents with progesterone-like activity, often defined by bioassay in rodents. Some of these drugs are 19-nortestosterone derivatives (eg, norethindrone) and some are relatively simple modifications of progesterone itself (eg, hydroxyprogesterone, medroxyprogesterone). Progestins were used extensively in the past in the treatment of threatened or habitual abortion. Studies showed excellent salvage of pregnancies treated with progestins compared to those not treated (eg, Jacobson, 1965). These studies did not, however, use randomization or matching techniques and did not use placebo controls. With the recognition that most first trimester pregnancy losses represent expulsion of an abnormal conceptus, progestin therapy of threatened abortion was largely abandoned. There have been those who contend, in fact, that progestin therapy might inhibit the natural completion of abortion, resulting in "missed abortion". A high incidence of missed abortion following a depot preparation of medroxyprogesterone acetate was reported in 1967 (Piver et al, 1967). It is possible that spontaneous expulsion of a dead fetus would be inhibited by progestin therapy; however, there was a mistaken belief, due to publications of this nature, that progestins (and by implication, progesterone) cause missed abortion; that is, cause the pregnancy to miscarry. Work on the first trimester effects of medroxyprogesterone acetate shows no influence of hormonal therapy on maternal urine or serum levels of hormones such as HCG, estradiol, and progesterone during the first half of pregnancy (Yovich et al, 1985; Willcox et al, 1985; Yovich et al, 1986). Medroxyprogesterone acetate is capable of supporting pregnancy in animals in place of luteal function (eg, Gadsby et al, 1983). Although placebo-controlled, randomized studies have not established that progestins prevent human miscarriage, animal studies and available human reports do not support the contention that progestins cause abortion.

Progestins may cause masculinization of female fetuses (Wilkins et al, 1958; Wilkins, 1960; Dyan and Rosa, 1981). This appears especially likely for testosterone-derived progestins such as norethindrone and ethisterone but has also been reported with the progesterone-derived progestins, medroxyprogesterone acetate and hydroxyprogesterone caproate. A variety of non-genital birth defects have been associated with first trimester use of progestins: such defects include neural tube defects, cardiac malformations, and skeletal anomalies (Dillon, 1970; Dillon, 1976; Heinonen et al, 1977; Corcoran and Entwistle, 1975; Harlap et al, 1975; Nora and Nora, 1973a,b; Nora et al, 1976; Nora et al, 1978); however, much of the reported experience in humans is limited by the unspecified nature of the drugs involved and by the frequency of early pregnancy treatment with multiple progestins and estrogens. The reported abnormalities have not yet shown a pattern or frequency of occurrence sufficient to conclude a causal role of progestins in the production of teratogenic effects. In spite of the inconclusive nature of the evidence, the Food and Drug Administration (FDA) has condemned the use of progestins as a group in pregnancy. Since this action, a study of progestins (chiefly medroxyprogesterone acetate) in 1608 first trimester pregnancies with bleeding showed no increase in anomalies compared to a control group of women with first trimester bleeding who did not receive progestins (Katz et al, 1985). The masculinization effect of progestins on female fetuses, the only complication for which there is compelling support, appears to occur infrequently with an incidence of perhaps 1% (Schardein, 1980).

It is important to remember that none of these data implicate progesterone itself. On theoretical grounds, exposure to progesterone during pregnancy should be innocuous, since all human pregnancies feature exposure to this hormone. There is no convincing evidence that progesterone vaginal suppositories elevate progesterone levels to dangerous levels or that any pregnancy complication should be expected from this therapy.

IIIC. Tubal surgery

Blockage of the fallopian tubes may in some instances be alleviated by surgery to remove the obstructing scar tissue or to resect an abnormal segment of tube with reanastomosis of the remaining segments. Lysis of adhesions can occassionally be accomplished through the laparoscope; however, in general procedures to correct tubal obstruction are major surgical operations. They are performed under general anesthesia and require several hours of operating time. The complications of general anesthesia, including drug reactions, cardiac depression, hypotension, aspiration, and death, do not appear to be different for infertility surgery than for surgery in general. Young, healthy individuals almost never suffer anesthesia complications such as these. Surgical complications such as injury to bowel, excessive blood loss, and infection are possible with any intraabdominal operation. There are no data specifically on the incidence of these adverse outcomes in tubal surgery, but it would be expected that the incidence would be very low. Because of the length of tubal surgery cases and the use of operating microscopes (requiring that tissue be held steadily for long periods), it is common for self-retaining retractors to be used in the abdomen. These have the potential to cause nerve compression injury, especially involving the ilioinguinal component of the femoral nerve (Meldrum, 1979; Hassan et al, 1986). Such injuries are infrequent and almost always reversible.

Surgery may cause scar tissue of its own and much effort has gone into developing procedures to prevent post-operative pelvic adhesions. Many fertility surgeons administer brief course of anti-inflammatory drugs, usually including a potent glucocorticoid such as dexamethasone. Such regimens have been shown to transiently blunt adrenal responsiveness to hypoglycemia in a minority of patients (Magyar et al, 1984). Although glucocorticoid therapy may entail complications such as poor wound healing and increased susceptibility to infection, the brief duration of drug administration is unlikely to be accompanied by such adverse effects. Anecdotal human and controlled animal experience (Luciano et al, 1983) suggests that intraperitoneal use of dextran results in decreased adhesion formation after surgery. As has been seen with dextran used during hysteroscopy, anaphylaxis may occur (Borton et al, 1983). The incidence of anaphylaxis after intravenous dextran has been estimated as 0.008% (Ring and Messmer, 1977). It is not known how often anaphylaxis occurs after intraperitoneal dextran, but it is not believed to be more often than after intravenous dextran. Intraperitoneal dextran may be associated with more mild side effects such as leakage of the material through the wound and painless labial swelling (Magyar et al, 1985). The incidence of these minor complications is less than 10%. If, however, dextran is continuously administered through an indwelling intraperitoneal catheter, there is a high incidence of abdominal pain, labial swelling, dyspnea, and pleural effusion (Gauwerky et al, 1986). It is unusual to see dextran administered in this fashion.

The complication of tubal surgery which is the most feared is ectopic pregnancy. In one series of ectopic pregnancies, 10.6% of patients had had previous pelvic surgery (Hassan, 1983). Although not all of these patients had tubal reconstructions, it stands to reason that tubal surgery would be at least as strong a predisposing factor to ectopic as other pelvic operations. It should be remembered that woman having tubal surgery are those with preexisting tubal disease and it may not be possible to determine whether a subsequent ectopic pregnancy is due to the effects of the surgery or the underlying disease. For example, in a series of 200 women who had conservative surgery for ectopic pregnancy (that is, the affected tube was repaired rather than removed), 122 subsequent pregnancies were reported. There were 24 ectopic pregnancies in this group for a rate of nearly 20%. Half of the ectopics, however, were in the tube that had not been involved by the original ectopic, suggesting that underlying tubal disease, rather than the effects of operating on the tube, were important factors in ectopic pregnancies in this group (Hallatt, 1986).

A number of investigators have reported ectopic pregnancy rates after tubal surgery:

Seiler, 1983	4%
Daniell et al, 1986	10%
Russell et al, 1986	17%

Henderson, 1984	17%
DeCherney and Kase, 1981	17%
Mage and Bruhat, 1983	20%
Gomel, 1978	31%
Mage and Bruhat, 1983	33%
Kelly, 1983	33%
Harris and Daniell, 1983	38%

Seiler's excellent results are attributable to the inclusion only of patients having a midsegment tubal ligation reversal. This procedure is generally believed to result in a greater degree of success than operations near either extremity of the fallopian tube.

The duplicate entry for Mage and Bruhat is due to the division of their patients according to whether or not a laser was used for the tubal surgery. The lower ectopic pregnancy rate was obtained using laser surgery. Before concluding that laser surgery reduces the rate of ectopic pregnancy, it should be noted that Kelly's 33% ectopic pregnancy rate was also obtained after laser surgery.

The issue of the safety of laser surgery merits discussing here. The laser is a tightly collected beam of light which is used to vaporize tissue. When a small spot size (ie, a narrow beam) is used, the laser vaporizes rapidly and deeply, acting like a knife. A larger spot size results is more dissipation of laser energy as heat and gives more of a cautery effect. Advocates of the laser advance this technique because of the ease of control of the amount of tissue destruction. Use of the laser either through the laparoscope or directly at laparotomy permits the destruction of endometriotic implants without injury to underlying structures and permits surgery on the fallopian tube with less (theoretical) likelihood of scar tissue formation. Others believe that improved results after laser surgery have not been documented at that the expense of the equipment cannot be justified.

Much of the work using laser through the laparoscope has involved the treatment of endometriosis and will be discussed below under that heading. Use of laser at laparotomy for tubal reconstructive surgery may be associated with complications specific for the laser such as inadvertent reflection of the laser beam resulting in damage to other tissues or in the starting of fires in the surgical drapes. The incidence of documented injury from laser surgery in the abdomen is, however, less than 0.5% (Daniell, 1984).

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IIID. Therapy of endometriosis

Endometriosis consists of implants of endometrial tissue outside the uterine cavity. These implants are most commonly found over the uterosacral ligaments and on the ovaries. Although it is not clear how endometriosis causes infertility or even how often it causes infertility, it is customary to treat endometriosis if the diagnosis is made, particularly in a woman who is having difficulty conceiving. The effectiveness of such treatment in facilitating pregnancy is an important issue but is beyond the scope of this discussion. Endometriosis therapy consists of either removal/desctruction of the endometriotic tissue or of suppression of the hormonal stimulation of all endometrial tissue. This latter treatment is tantamount to suppression of menstrual periods, since the endometrial tissue within the uterus responds in a manner similar to that of the abnormally located endometrial tissue of endometriosis.

1. Suppression of menses: Endometrial tissue, both within the endometrium and in endometriosis, is stimulated by estrogens. Endogenous estrogens are produced chiefly by the ovarian follicles under the influence of FSH. Reduction in FSH production, therefore, should reduce estrogen production and endometriosis stimulation. FSH production may be suppressed by a number of steroid hormones and their cogeners. Oral contraceptives, for example, have commonly been used to suppress FSH and have some activity in treating endometriosis. Oral contraceptives, however, contain estrogens and it is possible that the estrogen in these medications may to some degree stimulate the endometriosis. For this reason, oral contraceptives are not as popular as other therapies for use in severe endometriosis or in infertility patients.

A hormone which has become widely used in the suppression of endometriosis is danazol. This is an androgen which has been modified to reduce the masculinizing side effects of drugs of this class. Danazol does not appear to stimulate endometriosis and may, in fact, have a direct effect on eliminating the implants. Danazol, however, is expensive and has unpleasant side effects. Most women taking this drug experience bloating and weight gain of up to 25 pounds (Buttram et al, 1985). Other common side effects include muscle cramps, flattening of the breasts, hot flushes, oily skin, depression, acne, and hirsuitism (Buttram et al, 1985; Jelley and Magill, 1986). These effects are, in general, manifestations of the androgenicity of the drug or of the hypoestrogenism induced by it. More serious complications have been described with this agent. Four cases of thrombocytopenia in women using this agent were reported to the FDA (Arrowsmith and Dreis, 1986). Hepatotoxicity has been reported several times with elevations of hepatic transaminases (Nagata et al, 1981), frank hepatitis (Ohsawa and Iwashita, 1986; Boue et al, 1986), and hepatocellular carcinoma (Buamah, 1985). Serious hepatic dysfunction is, however, unusual in women on danazol.

There is no evidence that danazol therapy can cause persistent reproductive toxicity after the drug is stopped; however, inadvertent administration of danazol during pregnancy can cause masculinization of female fetuses (Duck and Katayama, 1981; Peress et al, 1982; Castro-Magana et al, 1981; Quagliarello and Greco, 1985; Kingsbury, 1985. Since danazol causes cessation of menses, a woman beginning the drug early in gestation may not realize for months that she is pregnant. It is advised, therefore, that danazol be started only after a normal menstrual period or after obtaining other evidence that the patient is not pregnant.

Analogues of GnRH have been studied in the therapy of endometriosis.

These agents interfere with the action of native GnRH resulting in decreased gonadotropins and therefore in hypoestrogenism. The analogue most extensively investigated in buserelin, which has been found as effective as danazol with comparable numbers of hypoestrogenic side effects (Yee, 1986; Franssen et al, 1986; Jelley and Magill, 1986). Buserelin therapy does not appear to result in as much acne, weight gain, nausea, or depression as does treatment with danazol (Jelley and Magill, 1986). It is not known whether serious complications of GnRH analogues will occur less often than those occurring with danazol. Due to the rarity of serious danazol complications, it is unlikely that this issue will be resolved without a large study population. A disadvantage of buserelin is that it must be given by injection or by the intranasal route. At this writing, GnRH analogue therapy for endometriosis is considered investigational.

2. Surgery: Removal of all endometriotic tissue is the most straightforward approach to therapy; however, the probable existence of microscopic implants casts doubt on the ability of surgery to establish a cure in all cases. Medical therapy, as described above, is favored unless bulky endometriotic disease is present or unless there are extensive pelvic adhesions which require lysis. The considerations pertaining to endometriosis surgery are similar to those discussed under tubal surgery above; however, there is currently considerable enthusiasm for attempting to ablate endometriosis through the laparoscope rather than by laparotomy. Because endometriosis may be located over vital structures such as bladder, ureter, and bowel, the laser has been favored by many surgeons as permitting ablation of implants without injury to adjacent or underlying tissue.

Early experience with laser laparoscopy in animals and humans suggested that the technique was, in fact, very safe (Daniell and Brown, 1982). Subsequent reports including larger numbers of procedures revealed that complications from laser laparoscopy occur, although serious complications are infrequent. In a series of 737 laser laparoscopy procedures, 3 bowel burns were noted, although all were managed by observation only. In the same series, there were 21 instances of intraabdominal bleeding as a result of the laser. A traditional cautery forcep was used to control the bleeding in 20 of these cases, but laparotomy was required in one of the patients (Martin, 1985). A series of 158 patients reported another 21 bleeding episodes; however, all were controlled without resorting to major surgery (Davis, 1986). In a group of 115 patients with laser laparoscopies for endometriosis, the pregnancy rate was 48% (Martin, 1986). Miscarriages occurred in 28% of these pregnancies and ectopic pregnancy occurred in 2% (which represented one patient). It appears, then, that laser laparoscopy is an acceptably safe tool for the treatment of endometriosis, although intraabdominal bleeding may require the use of traditional cautery for control. Based on the limited number of reports available, serious complications do not appear to occur more often than in laparoscopies in general.

IIIE. Artificial insemination

Artificial insemination involves the injection of semen or sperm into the cervical mucus or the uterine cavity of a woman. A distinction is made between insemination with the semen of the woman's husband (AIH) and insemination of donor semen (AID). AID is most commonly used when the woman's husband is infertile but may also be used when the husband carries a heritable disease or when blood type sensitization in the woman requires impregnation by a man of a specific blood type. AIH is used in some instances of male subfertility, although the effectiveness of AIH has been debated.

The major risk of AID is transmission of disease from the donor to the recipient. A number of pathogenic microorganisms have been identified in semen. These include chlamydia, a cause of pelvic infection (Bruce et al, 1981), Neisseria gonorrhoeae (Jennings et al, 1977; Garcia et al, 1981), cytomegalovirus, a potential cause of fetal illness (McGowan et al, 1983; Biggar et al, 1983; Lang and Kummer, 1972; Lang and Kummer, 1975; Lang et al, 1974); hepatitis B virus (Heathcote et al, 1974; Wright, 1975), and human immunodeficiency-associated virus (HIV), the agent of the acquired immunodeficiency syndrome (AIDS) (Ho et al, 1984; Zagury et al, 1984). It is clear that organisms present in semen gain access to the cervix and peritoneal cavity of the recipient woman; although, access to the peritoneal cavity appears to be much less common after intracervical insemination than after intrauterine insemination (Stone et al, 1986).

It is not surprising, then, that venereally-transmitted diseases have been documented in women as a result of AID. These diseases include gonorrhea (Chong and Taymor, 1975; Strickler et al, 1975; Fiumara, 1972), streptococcal pelvic infection (Kleegman, 1967), trichemonal vaginitis (Kleegman, 1967), Ureaplasma infection (Barwin, 1984), and AIDS (Stewart et al, 1985). There is also a case report of a man who contracted Reiter's syndrome from his wife who, although asymptomatic, had been exposed to this disorder through AID (Kingsley et al, 1985). It is not known if syphilis can be transmitted by AID (Mascola and Guinan, 1986). Herpes virus has not been found in the semen of affected men and it is not believed that this disorder can be transmitted by AID (Deture et al, 1978).

The incidence of transmission of disease by AID is unknown and certainly depends on the nature of the donor population and the type of screening tests employed. One report on 2308 AID procedures indicated that no sexually transmitted diseases had been encountered (Schlaff, 1986). Donors in this program were screened by medical history and serology, presumably for syphilis and HIV antibody. It does not appear practical to culture the urethra of each donor or to obtain blood for serologies every time a semen specimen is obtained. In addition, these tests would have to be run some days before specimen collection in order to have the results in time to use the specimen (since freshness of the semen is important in insemination success).

A possible alternative is the use of frozen ejaculates in insemination. With the semen preserved in this manner, there is time to obtain cultures either of the donor's urethra or of the semen itself. Serology tests can be performed and the ejaculate held until results are available. Because AIDS patients may not develop a positive antibody test for months after exposure to HIV, it has been suggested (Stewart et al, 1985) that HIV antibody tests be run on the donor three to six months after semen collection before the ejaculate is used. Although this may decrease the transmission of disease, it must be recognized that the pregnancy rates with frozen semen are only about one-third of those obtained with fresh ejaculates (Ball, 1986). It is believed by some authors (eg, Schlaff, 1986) that use of a reliable donor population is compatible with acceptably safe fresh semen donation.

Aside from the risks of viruses such as HIV or cytomegalovirus, there do not appear to be fetal risks from AID using either fresh or frozen semen (Fabro et al, 1985). Animal husbandry, in fact, relies heavily on the use of artificial insemination for the production of prize stock.

IIIF. Male genital surgery

Surgery on the genital tract of the male may be divided into that involving the duct system, used in instances of obstruction or congenital atresias, and that involving the venous system of the scrotal contents.

1. Genital duct surgery: Most surgery of this nature involves reanastomosis after vas ligation. The major problem with reversal of vasectomy is failure of the procedure to work. Operative infection and bleeding are possible but usually not serious. Microsurgery for developmental abnormalities has been described (Ross, 1983) and may be reasonably successful. 2. Varicocele ligation: The presence of enlargement of the internal spermatic or testicular veins may be associated with male infertility, presumably due to excessive temperature within the scotal sac (Lewis and Harrison, 1982). These dilated veins, called varicoceles, are the most common identified causes of male infertility (Dubin and Amelar, 1971; Greenberg et al, 1978). They may be removed either by ligation within the scrotum or by ligation higher up. Tulloch (1952) is credited with the first varicocelectomy, which was performed in an azoospermic man who responded to the therapy. This was a fortunate occurrence since azoospermia does not usually respond to this operation.

The major complication of varicocele ligation is postoperative hydrocele, a collection of fluid in the scrotum. The fluid collection may be due to inadvertent destruction of lymphatic drainage vessels during the procedure. In 83 patients with internal spermatic vein ligation without attention to preservation of lymphatics, the incidence of hydrocele was 7% (Szabo and Kessler, 1984). Attention to preservation of lymphatics resulted in an incidence of hydrocele of 3% (Dubin and Amelar, 1977, 1973). Other reports have given incidences of this complication as low as 1% (Brown, 1976) and as high as 25% (Wallijn and Desmet, 1978).

Testicular atrophy was at one time a complication of varicocele ligation, occurring in as many as 14% of cases. Improvements in surgical technique appear to have eliminated this complication (Fritjofsson et al, 1966).

More recent techniques for obliterating varicoceles have including embolization of the vessels with foreign material (White et al, 1981; Seyferth et al, 1981). In 260 men undergoing embolization with a fatty material, there was one patient with a severe reaction to the X-ray contrast and there were eight with varicose nodules with or without inflammation. These latter complications were minor and responded to anti-inflammatory drugs (Seyferth et al, 1981).

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IIIG. Drugs to improve male fertility

A number of different agents have been used in an attempt to optimize semen quality in infertile or subfertile men. These agent have been reviewed by Smith (1982) and include androgens, CC, HCG, HMG, GnRH, glucocorticoids, and a variety of other agents.

The rationale for giving androgens is to suppress the testis. Withdrawal of the androgens then might be accompanied by a rebound increase in spermatogenesis. It has been observed that some men are suppressed by androgens to azoospermia and may fail to rebound. It is not clear, however, if this is a complication of the drug treatment or of the primary testicular disorder for which the therapy was given (Smith et al, 1982). There are no reliable data with which to estimate whether androgens given for infertility may be associated with other complications. Provided that therapy is not prolonged, however, it appears unlikely that complications would occur.

The use of CC in oligospermic men is based on the antiestrogenic activity of this drug. There have been occasional reports of serious adverse effects of this therapy including a case of pulmonary embolism (Chamberlain and Cumming, 1986) and two cases of testicular germ cell tumors after therapy (Nilsson and Nilsson, 1985). The occurrence of such isolated cases may be coincidental and cannot be interpreted as indicating a risk of the therapy. It is considered unlikely that CC poses a significant health risk for men.

Glucocorticoids have been used in men to reduce the development or activity of antisperm antibodies. Glucocorticoids, given chronically, may be associated with adrenal suppression, osteoporosis, impaired glucose tolerance, psychosis, and other complications. Men receiving glucocorticoids for antisperm antibodies develop such complications as readily as any other patient (Ross, 1983).

Bromocriptine has been used with some success in uremic men with hypogonadism (Ermolenki et al, 1986). Although there are no studies on adverse effects of this type of therapy, side effects and potential complications should be the same as discussed above for this drug.

There are no data on possible complications of gonadotropin therapy in men. Such complications are considered unlikely.

IIIH. In vitro fertilization/embryo transfer

The ability to bypass the fallopian tube has been achieved with in vitro fertilization (IVF) and embryo transfer (ET). The technique involves obtaining an ovum by aspirating it from a preovulatory follicle. The ovum, obtained at laparoscopy in many cases, is exposed to sperm in vitro, where fertilization and early cleavage occurs. The conceptus undergoes two or more cell divisions in vitro and is then transfered to the uterus by injection through the cervical canal.

IVF involves several procedures with risks that have already been described. Laparoscopy, for example, was clearly the most complicated part of the procedure in early work. It is of interest that the use of anesthesia for what may be a long laparoscopic procedure does not appear to have adverse effects on the ovum obtained (Laufer et al, 1984). The replacement of laparoscopy by other methods of ovum retrieval will be discussed below. Other risks, however, attend the preparation of the ovary for egg retrieval. The original workers in IVF obtained eggs after spontaneous follicular development, since the patients involved had tubal disease, not disorders of ovulation. It has been shown, however, that the pregnancy rate after IVF-ET increases as more embryos are transferred in a given cycle (Laufer et al, 1984). Thus, it became desirable to cause more than one ovum to develop in each cycle. Trounson and coworkers (1981) are given credit for the first description of "controlled ovarian hyperstimulation", in which multiple follicles are induced to develop. Currently popular protocols for this controlled hyperstimulation involve CC-HMG (Yee and Vargyas, 1986) and HMG or FSH (Rosenwaks et al, 1986). With the use of these agents, there are accompanying risks as has been discussed above.

As more embryos are transfered, the incidence of multiple gestations increases. In a report from the Adelaide IVF program, the incidence of multifetal pregnancies was 25% (Kerin and Warnes, 1986). The Australian IVF Collaborative Group (1985) reported a twin rate of 19% and a triplet rate of 3%.

Complications attributable to the ET procedure have been reported. The catheter used to introduce the embryos into the uterus may result in trauma to the endometrium (Ng and Ratnam, 1985). Of more significance, however, is the possibility that the transferred embryos may find their way into the fallopian tube and implant there. The first successful IVF-ET pregnancy was, in fact, a tubal pregnancy (Steptoe and Edwards, 1976). Some programs report an ectopic pregnancy rate of 2-3% (Seppala, 1985; Kerin and Warnes, 1986); however, a review of the experience of a number of workers reported that 10% of IVF-ET pregnancies are extrauterine (Belaisch-Allart and Frydman, 1986). The placement of the ET catheter high in the uterus may predispose to ectopic pregnancy: Yovich et al (1985) reported a 17% ectopic rate with high placement as opposed to a 2% ectopic rate when the catheter was placed in the midcavity.

It has been noted that many IVF cycles demonstrate features of LPD (Frechtinger et al, 1982; Biggers, 1981). It has been proposed that aspiration of the follicle to obtain the ovum may damage the follicle or may remove too many granulosa cells. Indeed, work in monkeys supports the concept that follicle aspiration predisposes to LPD (Kreitman et al, 1981). Experience with human IVF cycles, however, suggest that the agents used to hyperstimulate the ovary are more likely to be responsible for luteal dysfunction than is aspiration (Vargyas et al, 1986). The miscarriage rate after establishment of clinical pregnancy has been reported to be around 20% (Kerin and Warnes, 1986), which is not markedly different from the abortion rate in other infertile women; however, miscarriage rates twice as high as those in normal populations have been described in IVF patients (Lancaster, 1985).

The obtaining of multiple ova leads to the possibility that more embryos will be generated than desired in a given IVF cycle. The cryopreservation of spare embryos for use in future cycles has been considered an important option in several programs. Thawing may fail to yield an intact embryo; however, the experience to date is that if the embryo successfully thaws, normal development is the rule (Trounson and Freemann, 1985). Of 16 pregnancies obtained with cryopreserved embryos in the Melbourne program, seven went on to give eight normal babies. One pregnancy resulted in a stillbirth at 20 weeks, and four pregnancies miscarried. The remaining four pregnancies were preceding normally at the time of the report (Trounson and Freemann, 1985).

Most IVF programs have noted that preterm delivery is more common in pregnancies after IVF-ET than in spontaneous pregnancies (Lancaster, 1985; Australian IVF Collaborative Group, 1985). In part this is due to the high incidence of multiple gestations; however, the increased prematurity rate is also seen in singletons. There is no apparent increase in the incidence of birth defects after IVF-ET (Australian IVF Collaborative Group, 1985; Lancaster, 1985; Kerin and Warnes, 1986) although the number of children studied after IVF-ET is still too small to detect a subtle increase in the rate of malformations. Psychosocial evaluation of 49 IVF children between the ages of 1 and 3 years revealed no problems attributable to the IVF-ET procedure. There were, however, two children with neurologic disorders with undoubtedly were associated with their very low birth weights (Mushin et al, 1985).

Recent developments in egg retrieval have included the use of ultrasound-guided aspiration of the follicle, obviating the need for laparoscopy. Lenz and coworkers (1981) are credited with development of the transabdominal approach to ultrasound-guided egg retrieval. Using this technique, ovum recovery and successful fertilization occur as often as with laparoscopic egg retrieval (Lewin et al, 1985). There is no apparent damage to the ovum from transabdominal retrieval (Wilkand et al, 1983). Since the aspirating needle may traverse the bladder, transient hematuria is seen with regularity after this procedure (Lenz and Lauritsen, 1982; Wilkand et al, 1983; Lenz, 1985). No major complications were seen in 230 patients reported by Lenz (1985). The aspirating needle may also be passed through the vagina if the follicles are more accessible from this vantage point (Lauritsen, 1983; Dellenbach et al, 1984). It is likely that ultrasound-guided aspiration of follicle will replace laparoscopy in many programs due to comparable results and lower cost, fewer discomforts, and less risk with the nonoperative approach (Hamberger et al, 1986).

III-I. Ovum/embryo donation

Ovum donation is a technique in which a donor woman is artificially inseminated with semen from an infertile woman's husband. The resulting embryo is flushed from the donor woman's uterus five to seven days later and is transfered to the infertile woman's uterus (or to the uterus of a surrogate). This procedure has been used to enable women without ovaries or without ova to carry a pregnancy. Although the donor supplies only the ovum (the sperm coming from the recipient's husband), it is really an embryo and not an ovum which is being transferred. Ovum donation has been most carefully described in a series of papers from one group (Bustillo et al, 1984a,b; Buster et al, 1985). Twenty-five embryos were recovered after 53 inseminations. Three intrauterine pregnancies and one ectopic pregnancy occurred after ET. Of the three intrauterine pregnancies, one aborted at 13 weeks and two went on to deliver normally. There was also a donor woman who retained the pregnancy after it failed to be flushed out. This pregnancy spontaneously aborted.

Although there is too little experience with ovum donation to estimate possible complications, the similarity of the ET procedures suggests that problems may be encountered similar to those seen in IVF-ET patients.

IIIJ. Gamete intrafallopian transfer

Credit is given to Asch et al (1984) for decribing the technique of combining ova and sperm in the fallopian tube. This technique, called gamete intrafallopian transfer (GIFT) is performed under laparoscopic guidance and therefore entails the risks, discomforts, and expense of that operation. In the first group of four patients at the University of Texas in San Antonio, there were three chemical pregnancies (defined as a positive HCG test). One of these pregnancies, which was a twin gestation, continued (Asch et al, 1985). A more extensive report from Brisbane described 19 pregnancies after 71 GIFT cycles. Three of these pregnancies aborted spontaneously. In the 16 continuing pregnancies there were three sets of twins (Molloy et al, 1987).

Although GIFT programs are new, it should be expected that multiple gestation will be the most hazardous problem encountered. The risk of ectopic pregnancy after this procedure is unknown but will certainly be more than zero.

IV. Research priorities

Some tests, for example, semen examination and cervical mucus examination, are viewed as completely safe and excite little research interest. In some cases, as discussed below, research efforts concern the accuracy of tests or the effectiveness of therapies rather than safety issues. For many of the diagnostic tests and most of the therapeutic procedures, however, there is room for the collection of additional data or the development of other techniques due to safety considerations.

1. Diagnostic modalities

Genital canal patency tests currently include the risk of post-procedure pelvic infection. This is presumed due to carriage of cervical organisms into the upper genital tract. Attempts have been made to screen patients at risk for this complication by obtaining cervical cultures and blood measurements of inflammatory response such as the white blood cell count and the erythrocyte sedimentation rate. In spite of these efforts, infection after HSG occurs. Future work in this area should be directed to the development of better tests to predict who should not have the procedure and to definition of whether antimicrobial prophylaxis will be effective in preventing infection.

The diagnosis of endometriosis by laparoscopy entails the risks of the operative procedure. The development of other tests for endometriosis would permit avoidance of surgery in at least some women. Although many infertility specialists believe it is necessary to visualize the extent of involvement of endometriosis, it is possible that suitably informed women might elect a trial of medical suppression of endometriosis without a "staging" laparoscopy. At this time, ultrasound offers the best hopes for a noninvasive test for endometriosis. Better defintion of ultrasound characteristics of endometriosis may be accompanied by the use of other imaging techniques, such as computerized tomography or magnetic resonance imaging, in an attempt to avoid diagnostic surgery in some women.

The avoidance of endometrial biopsy in a pregnant uterus is desirable. Current urine tests permit the diagnosis of pregnancy within two days of implantation. Thus, an endometrial biopsy performed just prior to the expected menstrual period may be preceded by an office pregnancy test to improve the safety of the procedure. Since some practitioners prefer endometrial biopsies in the midluteal phase, development of an earlier pregnancy test would be helpful.

Research priorities for male diagnostic tests center on the development of more accurate and informative test methods rather than on improving the safety of existing methods.

2. Therapeutic modalities

Ovulation induction entails risks to the woman of OHSS and risk to the woman and her offspring from multiple gestation. The monitoring of blood estrogen levels may minimize these complications but does not eliminate them. A more reliable method of monitoring or controlling the number of developing follicles is required. Ultrasound is a promising tool for detecting how many follicles have developed but does not provide information on how many follicles are being recruited early in the cycle.

An easy and accurate method of monitoring for OHSS and multiple follicle development would also discourage the unsupervised use of agents such as HMG. There are, apparently, still practitioners administering HMG with little if any monitoring and, as a result, women are still developing what should be preventable OHSS and high order multiple gestations. Daily blood or urine estrogens are somewhat cumbersome to arrange and may be omitted by the practitioner who does not have a regular program for HMG use. A simple office test would be a more convenient, and in the long run, a safer monitoring device for hyperstimulation.

Other ovulation inducing agents, without the same potential for OHSS and multiple gestation, may be developed. GnRH holds promise as one of these, but it remains to be established whether use of this agent will be safer or easier than the use of HMG.

The possibility that CC or HMG are associated with LPD requires additional investigation. If these agents do, in fact, impair luteal function, it may be necessary to alter treatment regimens, perhaps to routinely include the use of supplemental progesterone. A drug with some of the antiestrogenic action of CC but without the association with LPD would be desirable. Many antiestrogens have been developed without CC being replaced, suggesting that antiestrogenic action and LPD may go hand-in-hand; however, pharmacologic research may yield a drug which will divorce these two properties.

A prolactin-suppressing agent without the side effects of bromocriptine would be useful. Several candidates are being investigated at this time and future research may show one or more of them to be an adequate replacement for bromocriptine.

The utility of the laser in tubal surgery and in laparoscopic treatment of endometriosis requires additional investigation. Well-controlled studies comparing use of the laser with traditional instruments are important in determining whether this technique is worth the expense of the new instrumentation. These studies should also compare complication rates, include rates of recurrent scarring and ectopic pregnancy. It is possible that the laser will become an important component in reducing the risk of postoperative ectopic pregnancy; however, current data are insufficient for making this determination.

Endometriosis therapy with medication is on the verge of what may be an important breakthrough. Preliminary studies on GnRH analogs are encouraging; however, complete studies on safety and effectiveness of these medications must be completed. If GnRH analogs are as effective as danazol but have fewer side effects, many thousands of women will be spared the considerable discomforts of the current standard medical therapy. Additional research efforts should be directed towards developing an agent with direct effects on eliminating endometriosis, perhaps by augmentation of host immune functions. At the present time, endometriosis therapy in the infertile patient requires several months of medical therapy, often with associated side effects, during which time pregnancy is contraindicated. A more rapid, more comfortable treatment is clearly needed.

Artificial insemination research is being directed towards the identification of rapid tests for infectious diseases. If a semen sample could be screened within minutes for HIV, hepatitis B virus, gonorrhea, and perhaps other transmissible disorders, the specimen could be safely used without sacrificing the greater effectiveness of the fresh ejaculate. Future research may also identify a method of separating sperm from microorganisms so that only the gametes are placed into the recipient woman. Finally, the development of better cryopreservation techniques would be useful in permitting screening for infection without sacrificing the increased success of the unfrozen specimen.

Research efforts on drugs used in subfertile men are concentrating on identifying effective therapies rather than on improving the safety of existing therapies.

The development of IVF-ET, ovum donation, and GIFT has opened a new frontier in infertility research. There are large numbers of questions to be answered. With regard to potential complications of these procedures, future research will be directed to maximizing pregnancy rates while minimizing multiple gestation rates. Work on the ET aspect of IVF and ovum donation will need to concentrate on the prevention of ectopic pregnancy. IVF pregnancies must be examined to determine why preterm deliveries are increased and how this can be corrected.

As the use of cryopreserved embryos increases, there will be additional data on the normalcy of children handled in this manner. In addition, there should be research on manipulation of cells from the cryopreserved embryo, either for genetic diagnosis or for duplication of the embryo to increase pregnancy rates. Although manipulations of this sort have been successful in animals, it is not yet possible to conclude safety in humans.

It is of course recognized that the discussion of infertility treatments, particularly of IVF, ovum donation, and GIFT, entails ethical, legal, and sociologic issues. As the safety and effectiveness of these procedures becomes established, these other issues are likely to become the most urgent research priorities in this field.

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